Molecular assessment of atopic dermatitis and psoriasis samples collected using a non-invasive technique

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Introduction/Background: Updates in the molecular understanding of common and often debilitating skin diseases such as atopic dermatitis (AD) and psoriasis led to the development of multiple targeted systemic drugs. Optimal response to these medications relies on correct diagnosis, as well as clinical, personal, and molecular factors unique to each patient. Currently, unstandardized assessment of clinical characteristics and comorbidities drive the development of a therapeutic plan for patients with AD and psoriasis. The molecular mechanisms underlying each patient's disease are not routinely assessed when developing a treatment plan. This empirical approach to treatment selection delays optimal therapeutic response and leads to increased costs to healthcare systems. Therefore, incorporating molecular information from an individual patient's disease should inform better treatment decisions.

Previously, we presented the proof of concept for a non-invasive skin scraping sample collection technique by assessing gene expression differences of select genes of interest from psoriasis and AD samples using quantitative polymerase chain reaction. Indeed, candidate genes were differentially expressed in AD and psoriasis lesions relative to non-lesional skin and in AD relative to psoriasis lesions, demonstrating the feasibility of this collection technique. An algorithm based on the gene expression profiles of AD and psoriasis samples could be used to help guide therapy selection.

Objective: To assess the molecular profiles of AD and psoriasis samples collected using a non-invasive skin scraping method with the ultimate goal of developing and validating a molecular test for these common inflammatory skin diseases.

Methods: The superficial epidermis of lesional and non-lesional skin from patients with AD or psoriasis from three dermatology centers in the United States was collected by gently scraping the skin ten times with a curette and immediately preserving the sample in a proprietary buffer**.** RNA isolated from samples was stored at -80°C until further use. Library preparation and next generation RNA sequencing was performed using the Ion AmpliSeq Transcriptome Human Gene Expression panel on the S5XL sequencer (ThermoFisher). Differential expression of genes was assessed using DESeq2; Metascape was used to assess enriched gene ontology of differentially expressed genes.

Results: When comparing AD lesional and non-lesional skin, 1,633 transcripts were differentially expressed (absolute value of log2fold change >1.0 and p_{adj} <.05). Additionally, 4,468 transcripts were differentially expressed between psoriasis lesional and non-lesional skin. Further, principal component analysis demonstrated that lesional and non-lesional samples for both AD and psoriasis could be distinguished by their respective gene expression profiles. Gene ontology enrichment analysis revealed that innate and adaptive immune system and cytokine signaling genes were among the most common types of differentially expressed genes between lesional and non-lesional samples. Moreover, gene expression differed between lesional AD and psoriasis samples.

Conclusions: These results suggest that a molecular test could be developed from AD and psoriasis samples collected by a non-invasive scraping technique. Further, clinical correlation

with therapeutic outcomes may be used in conjunction with molecular profiles to develop an algorithm to predict therapeutic response in these common inflammatory skin diseases.

Keywords: personalized medicine, molecular testing