Gene Expression Differences Identified in Skin Samples of Early-Stage Mycosis Fungoides, Atopic Dermatitis, and Psoriasis.

Aaron S. Farberg1,2, Matthew S. Goldberg1, Ann P. Quick3, Olga Zolotchevskaya4, Jeff Wilkinson5, Jonathan I. Silverberg4, Peter A. Lio5, John Koo5, Jeffrey Weinberg5, Mark Lebwohl7

1 - Baylor Scott & White Health System, Dallas, TX; 2 - Bare Dermatology, Dallas, TX; 3 - Castle Biosciences, Inc, Friendswood, TX; 4 - The George Washington University School of Medicine and Health Sciences, Washington, DC; 5 - Northwestern Feinberg School of Medicine, Chicago, IL; 6 - University of California San Francisco School of Medicine, San Francisco, CA; 7 - Icahn School of Medicine at Mount Sinai, New York, NY.

Background

- Updates in the molecular understanding of common and often debilitating skin diseases such as atopic dermatitis (AD) and psoriasis (PSO) led to the development of multiple targeted systemic drugs.1,2
- Yet, molecular heterogeneity contributes to inconsistent clinical presentation and therapeutic response. Therefore, understanding a patient’s personalized molecular profile may be important for determining the ideal therapy.3,4
- Further, systemic treatment of presumed AD or PSO can lead to delays in both diagnosis and proper treatment of patients with a true diagnosis of mycosis fungoides (MF) – a potentially dangerous clinical mimic of AD and PSO that requires a rigorous histologic and molecular workup to diagnose.5,6
- Therefore, a non-invasive method to distinguish MF from AD and PSO could accelerate accurate diagnoses and avoid inappropriate treatment of MF.
- We have previously discovered transcriptomic differences in MF and PSO samples obtained by a non-invasive scraping technique.7 However, this technique has not been used to assess differences in gene expression profiles of MF samples.

Objective

- To identify gene expression differences based on diagnosis of MF, AD, or PSO and response to targeted systemic AD or PSO therapies.

Methods

- Lesional basal samples were assessed from 76 patients (AD, n=24; PSO, n=48; and MF, n=4) enrolled in one of two IRB-approved studies (IDENTITY or SIGNAL).8-10
- Transcriptome Human Gene Expression panel and results Samples run on AmpliSeq Transcriptome Human Gene Expression panel and results correlated with therapeutic outcomes.
- Baseline samples were assessed from 76 patients (AD, n=24; PSO, n=48; and MF, n=4).
- Lesional skin samples were collected by gently scraping the skin ten times with a curette and immediately preserving in a proprietary buffer (Figure 1).
- Library preparation and next generation RNA sequencing was performed using the Ion AmpliSeq Transcriptome Human Gene Expression panel on the S5 Prime sequencer (ThermoFisher) for all samples.
- Clinical response to a subset of AD patients taking dupilumab was further assessed over 3 months using the eczema area and severity index (EASI).

Results

- Library preparation and next generation RNA sequencing was performed using the Ion AmpliSeq Transcriptome Human Gene Expression panel on the S5 Prime sequencer (ThermoFisher).
- Clinical response to a subset of AD patients taking dupilumab was further assessed over 3 months using the eczema area and severity index (EASI).
- Gene expression was compared between MF, AD, and PSO. 1 chronic hand eczema sample and 1 psoriasis sample from a patient with concomitant eczema were excluded from diagnostic gene expression analysis. Further, gene expression was assessed based on response to therapy for the subset of AD patients taking dupilumab with 3 months follow-up.
- Genes were considered differentially expressed if there was a log2 fold change >1.0 (and pad) ≥ 0.

Conclusions

- A robust gene expression is obtained from lesional PSO, AD, and MF samples collected by non-invasive skin scraping.
- Gene expression differences are observed between PSO, AD, and MF lesions.
- AD lesions from super-responders to dupilumab exhibit distinct gene expression.
- A non-invasive molecular test is being developed to
- Distinguish between AD, PSO, and MF.
- Identify super-responders to the targeted AD therapy dupilumab.

References


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