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

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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.[1,2,3]
- Yet, molecular heterogeneity contributes to inconsistent clinical presentation and therapeutic response. Therefore, understanding a patients' personalized molecular profile may be important for determining the ideal therapy.[4,5]
- 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. [6,7]
- 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 shown transcriptomic differences in AD and PSO samples obtained by a non-invasive scraping technique.[8] However, this technique has not been used to assess differences in gene expression profiles of MF samples.

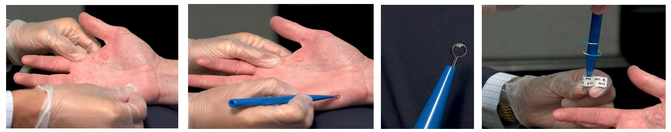
Objective

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

Methods

- Lesional baseline 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-MF).
- The superficial epidermis was collected by gently scraping the skin ten times with a curette and immediately preserving in a proprietary buffer (Figure 1).

Figure 1. Non-invasive Scraping Method to Collect Atopic Dermatitis, Psoriasis, and Mycosis Fungoides Samples

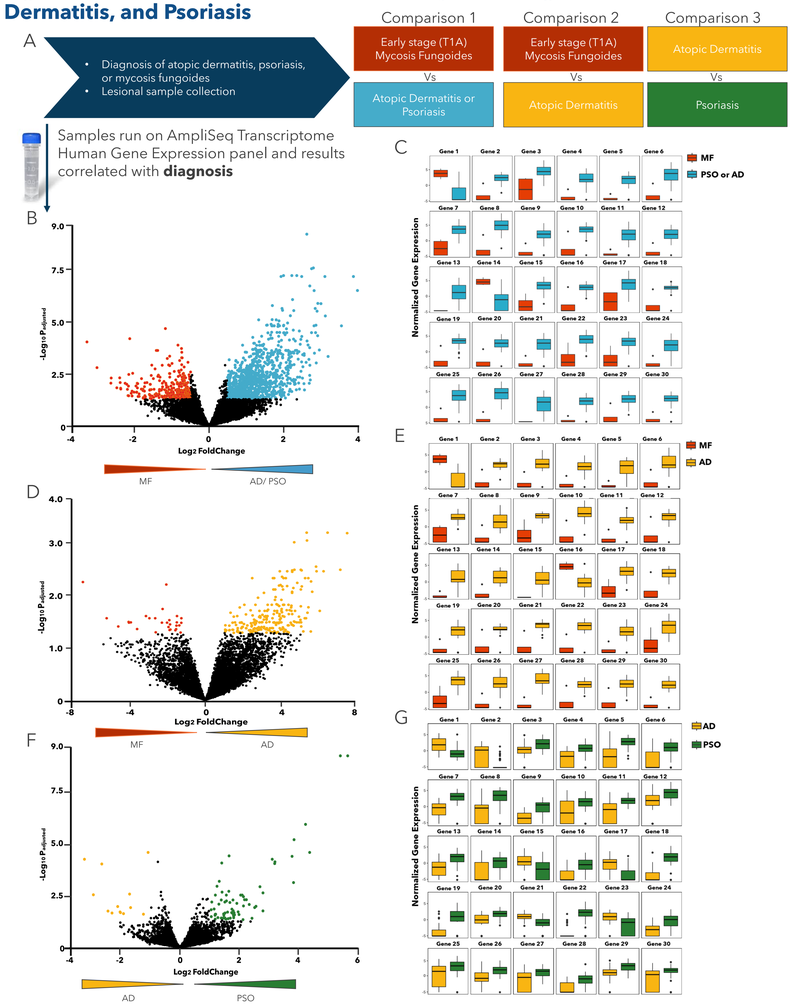


1. Skin prep – clean with alcohol swab
2. Gentle scraping with curette 10 times
3. Quality check
4. Storage in RNA-preserving buffer

- 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 log2fold change >|1.0| and padj <.05.

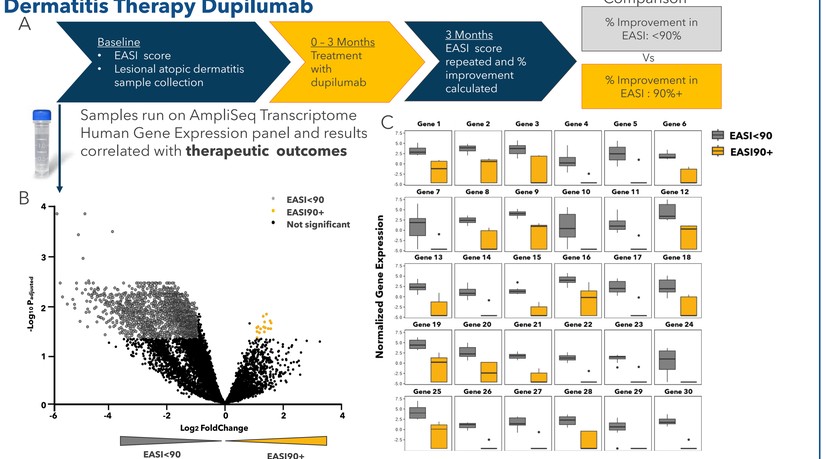
Results

Figure 2. Gene Expression Differences in Mycosis Fungoides, Atopic Dermatitis, and Psoriasis



A) Workflow. **B**) Genes were differentially expressed in lesional skin samples from MF compared to PSO and AD. **C**) Top 30 differentially expressed gene distributions for MF vs AD and PSO. **D**) Differentially expressed genes in lesional skin samples from MF compared to AD alone with top 30 differentially expressed distributions (**E**). **F**) Differentially expressed genes in lesional skin samples from PSO compared to AD with top 30 differentially expressed gene distributions (**G**). AD, atopic dermatitis; MF, mycosis fungoides, PSO, psoriasis.

Figure 3. Gene Expression Differences in Super-responders to the Atopic Dermatitis Therapy Dupilumab



A) Workflow. **B**) Genes were differentially expressed in baseline skin scrapings obtained from super-responders (EASI90+ response at 3 months, n=5) to dupilumab (blocks both IL-4 and IL-13 signaling) compared to those with EASI<90 (n=8) response. **C**) Top 30 differentially expressed gene distributions. EASI, eczema area and severity index; EASI90+, 90% or greater improvement in EASI; EASI<90, less than 90% improvement in EASI.

Conclusions

- 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.

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