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

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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.[1,2,3]
- Optimal response to these medications relies on correct diagnosis, as well as clinical, personal, and molecular factors unique to each patient. Currently, however, unstandardized assessment of clinical characteristics and comorbidities drives the development of a therapeutic plan for patients with AD and psoriasis. On the other hand, the molecular mechanisms underlying each patient's disease are not routinely considered when developing a treatment plan.[4,5]
- An empirical approach to treatment selection could lead to delay in appropriate treatment of AD or psoriasis and increased cost to healthcare systems.[6] Therefore, **understanding individual patient's disease at the molecular level** could better inform treatment decisions.
- Previously, we demonstrated the feasibility of a novel non-invasive 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 the sample collection technique.[7]
- However, a molecular assessment of **gene expression from skin scrapings of AD and psoriasis** could identify additional genes which could be used in an algorithm to **guide therapeutic selection**.

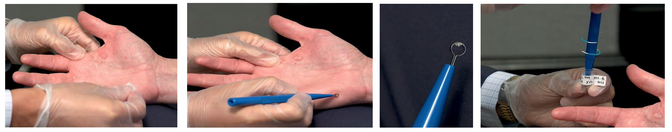
Objective

- To obtain a molecular profile from AD and psoriasis samples collected using a non-invasive sample collection technique with the goal of developing a test to guide therapy selection for AD and psoriasis.

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 in a proprietary buffer.

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

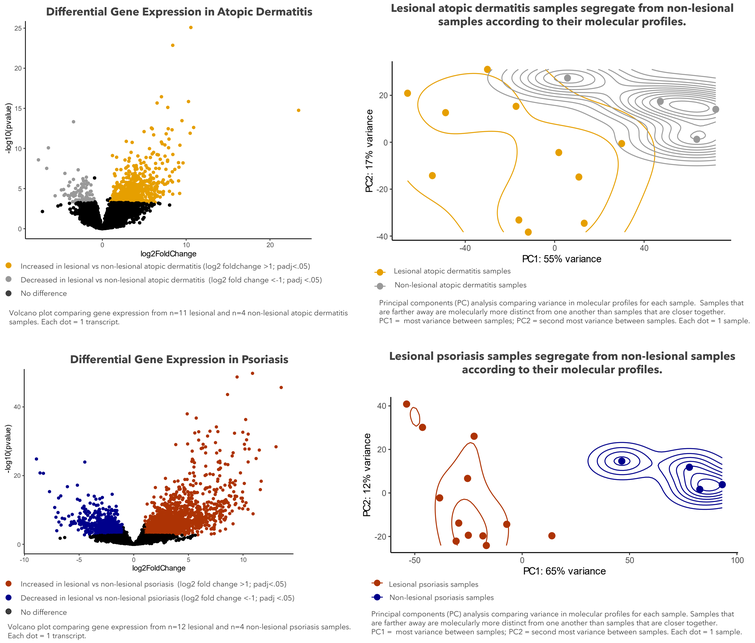


1. Skin prep – clean with alcohol swab
2. Gentle scraping with curette 10 times
3. Quality check
4. Storage in RNA-preserving buffer

- Samples were shipped at ambient temperature and frozen at -80º C upon receipt. RNA was isolated, and next generation sequencing was performed using Ampliseq (ThermoFisher).
- Differential expression of genes for 11 AD lesional and 4 non-lesional samples and 12 psoriasis lesional and 4 non-lesional samples was assessed using DESeq2 and enrichment of differentially expressed genes was determined using Metascape.

Results

Figure 2. Genes are Differentially Expressed in Lesional and Non-lesional Skin from Patients with Atopic Dermatitis or Psoriasis



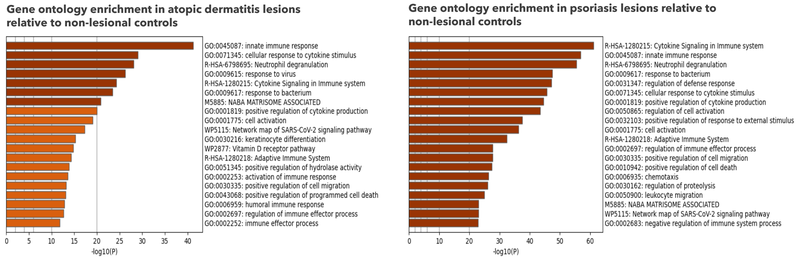
Volcano plot comparing gene expression from n=11 lesional and n=4 non-lesional atopic dermatitis samples. Each dot = 1 transcript.

Principal components (PC) analysis comparing variance in molecular profiles for each sample. Samples that are farther away are molecularly more distinct from one another than samples that are closer together. PC1 = most variance between samples; PC2 = second most variance between samples. Each dot = 1 sample.

Volcano plot comparing gene expression from n=12 lesional and n=4 non-lesional psoriasis samples. Each dot = 1 transcript.

Principal components (PC) analysis comparing variance in molecular profiles for each sample. Samples that are farther away are molecularly more distinct from one another than samples that are closer together. PC1 = most variance between samples; PC2 = second most variance between samples. Each dot = 1 sample.

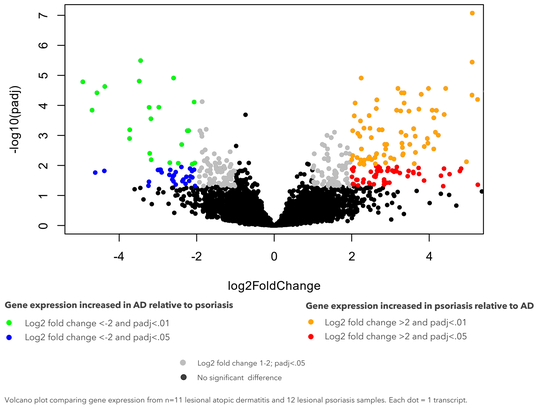
Figure 3. Immune and Inflammatory Pathways are Enriched in Atopic Dermatitis and Psoriasis Lesions



Gene ontology pathways enriched in Metascape analysis of top differentially expressed genes (log2 fold change >1 and padj<.01) from n=11 lesional vs n=4 non-lesional atopic dermatitis samples.

Gene ontology pathways enriched in Metascape analysis of top differentially expressed genes (log2 fold change >1 and padj<.01) from n=12 lesional vs n=4 non-lesional psoriasis samples.

Figure 4. Genes are Differentially Expressed Between Atopic Dermatitis and Psoriasis Lesions



Volcano plot comparing gene expression from n=11 lesional atopic dermatitis and 12 lesional psoriasis samples. Each dot = 1 transcript.

Conclusions

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 or algorithms to predict therapeutic response in these common inflammatory skin diseases.

References

1. David E. *et al. Clin Exp Allergy*. 2023;53(2):156-172.
2. Silverberg JI *et al. J Eur Acad Dermatol Venereol*. 2021; 35(9):1797-1810.
3. Armstrong A and Read C. JAMA, 2020;323(19):1945-1960.
4. Kaushik S and Lebwohl M. *J Am Acad Dermatol*. 2019; 80(1):27-40.
5. Aggarwal P *et al. Dermatol Ther (Heidelb).* 2022; doi:10.1007/s13555-022-00683-4.
6. Mathur S and Sutton J, *Biomed Rep*. 2017; 7(1):3-5.
7. Quick *et al.*, Revolutionizing AD. 2022.

Disclosures

- APQ, MSG, and JW are employees and shareholders of Castle Biosciences, Inc.
- ASF is a consultant for Castle Biosciences, Inc. and on the advisory board for Eli Lilly, Sun Pharma, Orthodermatologics, Boehringer Ingelheim, Incyte, Amgen, Galderma, Novartis and Pfizer.
- JIS is a consultant and/or advisor for Abbvie, Afyx, Aobiome, Arena, Asana, Aslan, BioMX, Biosion, Bluefin, Bodewell, Boehringer-Ingelheim, Cara, Castle Biosciences, Celgene, Connect Biopharma, Dermavant, Dermira, Dermtech, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo Pharma, Luna, Menlo, Novartis, Optum, Pfizer, RAPT, Regeneron, Sanofi-Genzyme, Shaperon, Sidekick Health; speaker for Abbvie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from Galderma, Pfizer