Feasibility of a novel, non-invasive sample collection technique to develop a molecular test guiding therapeutic selection for patients with atopic dermatitis and psoriasis

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Background

- Recent advances in the understanding of the molecular pathways underlying the development of atopic dermatitis (AD) led to the development of multiple novel systemic drugs targeting those pathways.1,2
- As more therapeutics are approved for treatment of AD, it will be important to make informed decisions about each individual patient’s therapeutic plan. However, choosing a systemic therapy for AD may not be straightforward.
- Currently approved therapeutics target IL-4 and IL-13 cytokines or the JAK/STAT pathway. Additionally, clinical trials show promise for therapeutic options targeting IL-31, CCR4, Ox40/Ox40L, etc.1,2,3
- Further confounding therapeutic selection, a subset of AD can mimic psoriasis. A recent study suggests that clinicians treat these cases empirically more often than consulting pathology.4 This is likely because biopsies are moderately invasive and can be inconclusive in many of these cases.
- A trial-and-error approach could lead to delay in appropriate use of AD or psoriasis treatments that increased cost to healthcare systems.5 Therefore, understanding individual patient’s disease at the molecular level could better inform treatment decisions.
- However, developing a test to incorporate each patient’s personal molecular biology into guiding therapeutic selection requires a clinically feasible test.

Objective

- To determine the feasibility of a quick, intuitive, non-invasive skin scraping technique to yield sufficient RNA to assess differentially expressed molecular biomarkers in the epidermis of patients with atopic dermatitis and psoriasis.

Methods

- The superficial epidermis of lesional and non-lesional skin from 20 patients with AD and 20 patients with psoriasis from two dermatology centers in the United States was collected by gently scraping the skin ten times with a curette and immediately preserving in a proprietary buffered fixative.
- Samples were shipped at ambient temperature and frozen at -80 degrees Celsius upon receipt. RNA was isolated, converted to cDNA; pre-amplified, and run on TaqMan OpenArray Real-Time PCR plates to assess relative gene expression of 28 genes by two separate operators. A log2 fold change >1 was considered an increase and a log2 fold change <1 was considered a decrease in gene expression.

Results

- Compared to lesional psoriasis, lesional AD samples exhibited increased expression of seven genes (circles above red line) and decreased expression of three genes (circles below blue line).
- Two of the seven genes with increased expression in lesional AD also demonstrated increased expression in non-lesional AD relative to non-lesional psoriasis samples (squares above mid line). One gene had reduced non-lesional expression (square before blue line).

Conclusions

- A non-invasive skin scraping technique produces sufficient RNA to assess reproducible gene expression by quantitative RT-PCR in lesional and non-lesional AD and psoriasis for the purposes of developing a gene expression profile to help guide therapeutic decision-making.

References


Disclosures

- APQ, MSG, and JW are employees and shareholders of Castle Biosciences, Inc.
- AGF is a consultant for Castle Biosciences, Inc. and on the advisory board for Eli Lilly, Sun Pharma, Orthodermatologics, Boehringer Ingelheim, Inc., Aymo, Galderma, Bausch & Lomb and Pfizer.
- JW is a consultant and/or advisor for Abbvie, Alny, Adavene, Area, Apea, Adam, Abott, Boehringer Ingelheim, Cari, Castle Biosciences, Calgene, Connect Biopharma, Dermavant, Dermira, Dermtech, Eli Lilly, Galderma, GaldermaCyclo, Insys, Kirin, Leo Pharma, Lusa, Merixi, Novartis, Optum, Pfizer, Rapt, Regeneron, Sandhagen, Shapero, Siddans Health; speaker for Abbvie, Eli Lilly, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from: Galderma, Pfizer.