MIND.PX

PERSONALIZED MEDICINE FOR PSORIASIS BIOLOGIC TREATMENT

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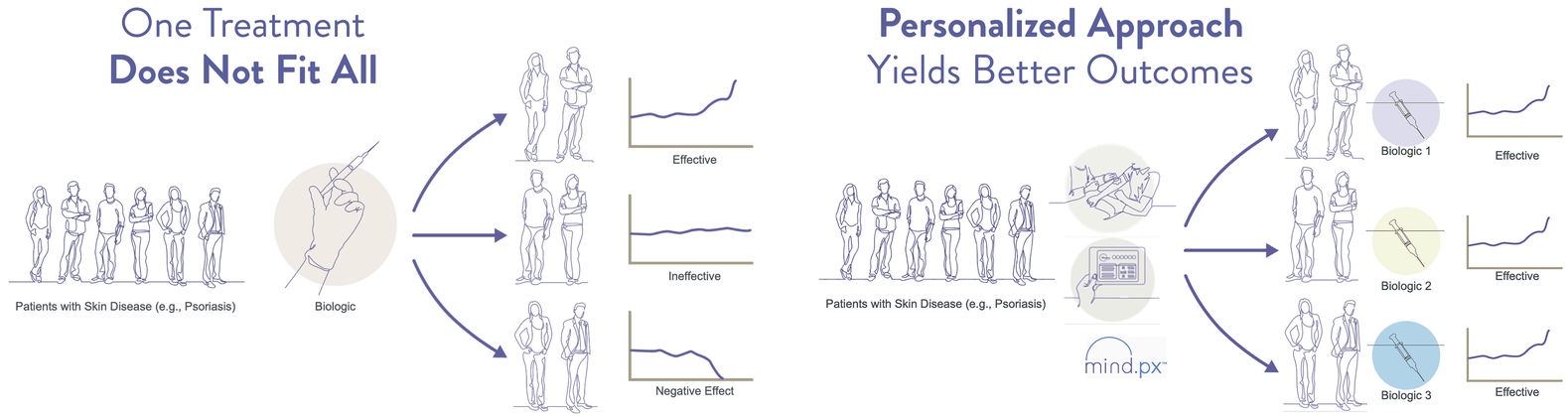
SYNOPSIS In the United States, psoriasis affects upward of 3% of the population, leading to healthcare costs of >$110 billion annually. The emergence of targeted biologic treatments has revolutionized the management of moderate to severe psoriasis patients, with impressive results. However, these clinical gains have come with a concomitant dramatic increase in the spending on higher priced biologic drugs. A personalized approach allows clinicians to prescribe the best medication, the first time. Patient outcomes quickly improve, without incurring the excess cost associated with a trial-and-error approach.



OBJECTIVE

To develop and validate a machine learning-based classifier that can predict if a psoriasis patient will respond to a specific biologic drug class prior to drug exposure.

METHODS

Transcriptomes were collected from subjects (N=232) with a psoriasis diagnosis using a proprietary Dermal Biomarker Patch kit (Figure 1A) that allows simple, rapid, and painless extraction of RNA from the skin (Figure 1B). Patient PASI scores were measured at baseline as well as weeks 12 and 16 after drug exposure. Transcriptomes were analyzed using next-generation sequencing (NGS) following standard protocols. The resulting data set (transcriptomic data and clinical outcomes) was used to train and prospectively validate a machine learning-based classifier for each class of biologic (TNFαi, IL-17i, IL-23i).

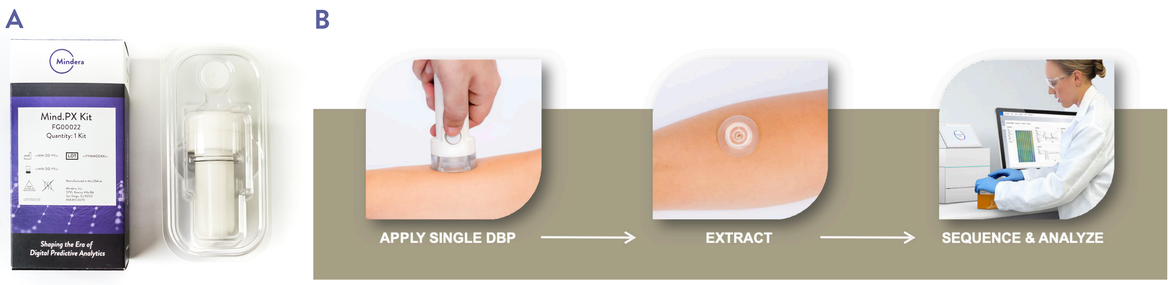


FIGURE 1. (A) Mind.Px kit. (B) Dermal Biomarker Patch workflow.

RESULTS

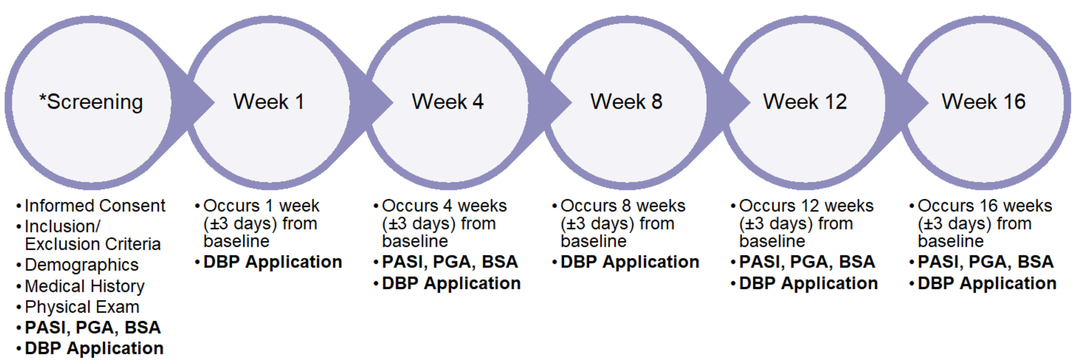
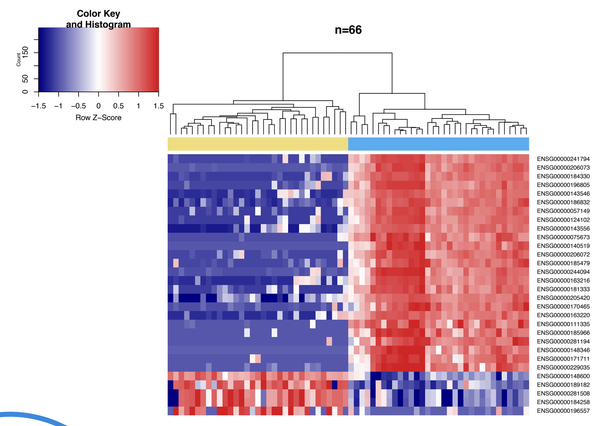
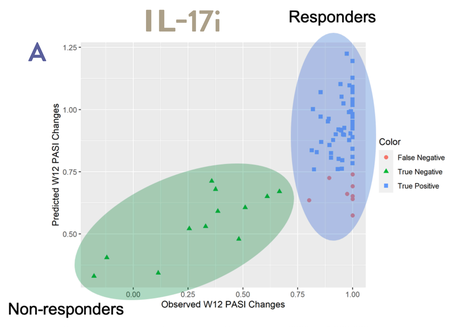


FIGURE 2. STAMP trial design. All enrolled subjects were not actively treated with topical medication on the study lesion and had not been dosed with any systemic medication for their psoriasis for at least 2 weeks.

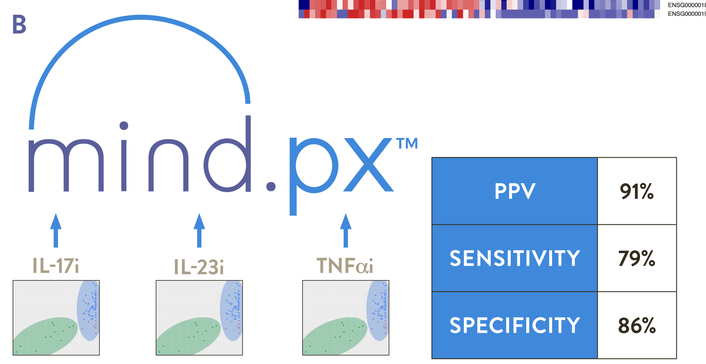
FIGURE 3. Preliminary evaluation of the psoriatic transcriptome obtained using the Mind.Px kit. In this data set (N=66), patient lesional and non-lesional transcriptomes were compared to confirm the analytical validity of the Mind.Px kit. On average, transcriptomes of >7,000 transcripts were obtained, of which ~1,500 transcripts were differentially regulated in lesional skin. Unsupervised clustering of the highest variance genes showed tremendous separation between lesional and non-lesional skin.





Source: Tomalin LE, et al, *J Allergy Clin Immunol*, 2020, 145:922-932.

PPV	BALANCED ACCURACY
>90%	>93%



PPV	91%
SENSITIVITY	79%
SPECIFICITY	86%

FIGURE 4. (A) IL-17i classifier development. Using a machine learning method that combines baseline transcriptome data with clinical outcomes as defined by W12 PASI, we have validated a classifier that predicts patient response to IL-17i biologics with high positive predictive value and high accuracy. (B) Combining individual classifiers for each of the three biologic classes (N=232 patients) yields the Mind.Px machine learning-based algorithm that predicts patient response to all biologic drug classes with high-positive predictive value (91%), sensitivity (79%), and specificity (86%).

CONCLUSION

INTELLIGENTLY, CONFIDENTLY CHOOSE PSORIASIS BIOLOGIC

By combining Mindera Health Dermal Biomarker Patch technology with machine learning methods, we developed a precision medicine test (Mind.Px) that can:

- accurately predict psoriasis-patient response to biologic class (TNFαi, IL-17i, or IL-23i) prior to drug exposure
- prescribe patients the right biologic the first time, for improved outcomes and tremendous cost-savings
- minimize the trial-and-error approach to psoriasis treatment

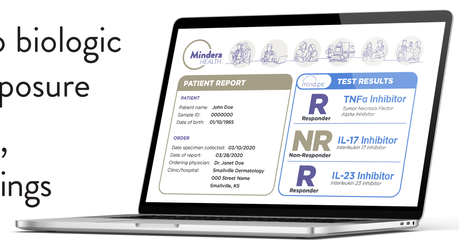


FIGURE 5. Sample Mind.Px test report showing patient response to TNFαi, IL-17i, and IL-23i biologics.

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A DERMAL BIOMARKER PATCH DISPLAYS EXCELLENT ANALYTICAL PERFORMANCE AND OUTPERFORMS TAPE STRIPPING IN PSORIATIC SKIN

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SYNOPSIS

The Dermal Biomarker Patch (DBP) platform efficiently captures transcriptomes of >7,000 biomarkers from the lesional skin of psoriasis patients in sufficient quantities for next-generation sequencing protocols. There was no significant body-site variation observed, in contrast to stratum corneum tape stripping.* This platform makes precision medicine in dermatology a reality. It provides a powerful tool for doctors, researchers, and patients to better understand the skin.

OBJECTIVE

To demonstrate the ability of the Mindera Health DBP to extract actionable quantities of mRNA from lesional skin of psoriasis patients, and explore the body-site dependence of this method.

METHODS

Using the DBP, a total of 416 transcriptomes were collected from 24 different body areas; each transcriptome was comprised of ~7,000 biomarkers. Samples were collected from research sites (N=15) under an IRB-approved protocol. After collection, samples were placed in a storage buffer between 2–8°C for transport and processing.

Once received, next generation sequencing (NGS) was performed according to standard procedures. Measurements were made of the gene detection rate and mRNA yield. Additionally, a subset of samples was analyzed at various time points after sample collection (1-10 days) to determine mRNA stability during storage and transport.

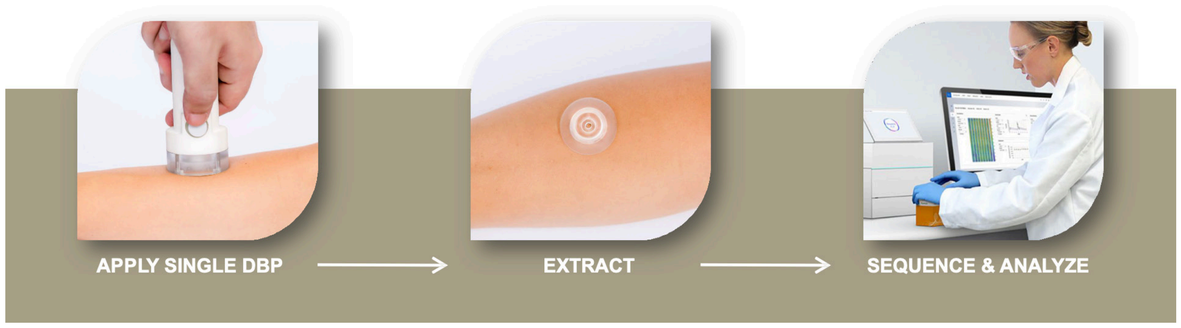

FIGURE 1. Dermal Biomarker Patch workflow.

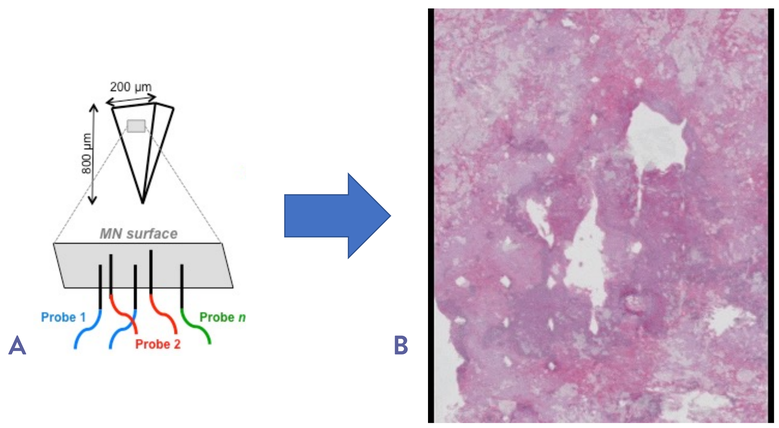

FIGURE 2. (A) Graphical depiction of DBP micro-projections. These projections are chemically modified to specifically bind to mRNA in the skin. (B) *En face* histology of DBP application. To assess the depth of penetration by the DBP, *ex vivo* skin samples were sliced *en face* and resulting puncture sites were quantified. On average, >90% of the DBP projections penetrated 350-400 µm into the skin.

RESULTS

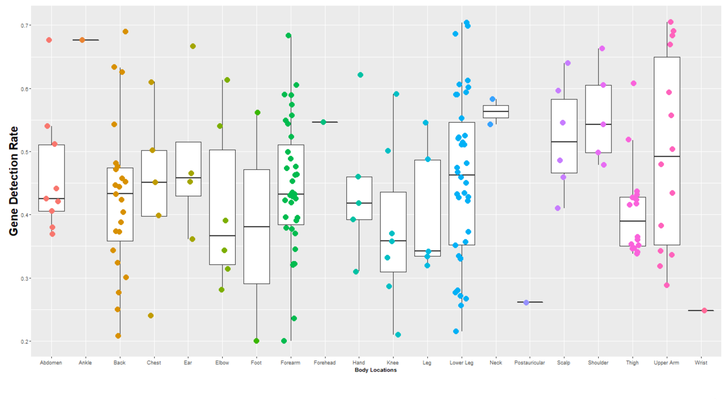

FIGURE 3. Gene detection rates from various body sites (N = 416). The gene detection rate ranged from 1.1% to 76.2%. The average gene detection rate was 43.3%. Based on a ≥20% gene detection rate acceptance criterion, >96% of the samples passed quality control metrics. Statistical analysis of the data set demonstrated no statistically significant difference observed between body sites (ANOVA, p=0.342), in contrast to previously published data using stratum corneum tape stripping.*

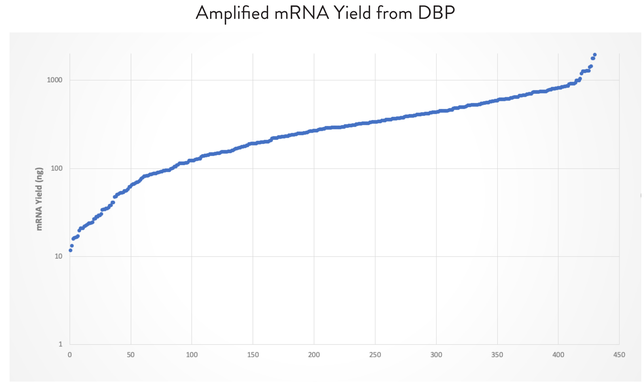

FIGURE 4. Yield of mRNA extracted from DBPs (N=412). The acceptance level for minimum concentration was determined to be 2-5 ng of amplified RNA at a concentration of 0.2 ng/µL. The yields of amplified mRNA ranged from 12–2,240 ng with an average yield of 360 ng, >100-times larger than the published average yields from stratum corneum tape stripping.* All samples passed the acceptance criterion of >4 ng and yielded acceptable results in downstream sequencing.

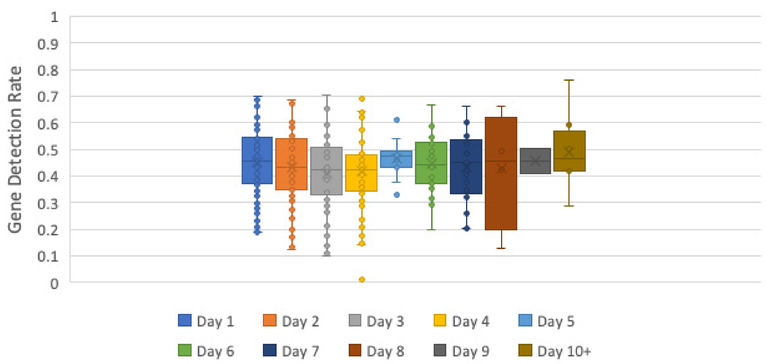

FIGURE 5. Influence of time between collection and processing on quality of DBP RNA-Seq data. A subset of 373 psoriasis skin samples was collected from research sites, stored in storage buffer at 2–8°C, and transported in an insulated shipper system at 2–8°C overnight for downstream analysis. To substantiate mRNA stability, the gene detection rates were determined for samples stored from 1 day to 10+ days. A total of 94.7% of the samples exceeded the QC threshold of 20% gene detection.

CONCLUSION

The Mindera Health Dermal Biomarker Patch platform has been proven to reliably extract the skin transcriptome in a minimally invasive manner. Success in psoriasis patients includes:

- highly reproducible efficiency of extraction
- excellent mRNA yields suitable for RNA-Seq protocols
- >96% of samples passing quality control metrics
- no body-site bias in transcriptome extraction

Funding for this project was provided by Mindera Health.

* Wong R, Tran V, Talwalker S, Benson NR. Analysis of RNA recovery and gene expression in the epidermis using non-invasive tape stripping. *J Dermatol Sci.* 2006, 44(2):81-92.