Tape-strip transcriptomics identify immune signatures in cutaneous T-cell lymphoma distinct from benign inflammatory skin diseases

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Background: Primary cutaneous T-cell lymphomas (CTCL), particularly in their early stages, frequently present with clinical and histopathologic features that overlap with atopic dermatitis (AD) and psoriasis, contributing to diagnostic delay and ineffective, or even deleterious, treatment approaches. Minimally invasive molecular tests capable of distinguishing CTCL from benign inflammatory dermatoses are thus urgently needed.

Objectives: We sought to determine whether tape-strip transcriptomics can detect disease-specific signatures distinguishing early-stage CTCL from AD, psoriasis, and healthy control (HC) skin.

Methods: Bulk RNA sequencing was performed on lesional and nonlesional tape strips from skin of patients with mycosis fungoides (MF; n = 18), AD (n = 36), psoriasis (n = 32), and HC (n = 30).

Results: Principal component analysis revealed distinct clustering of MF, AD, and psoriasis lesional skin relative to HC. MF displayed a mixed immune profile, contrasting with the strong T_H2 and T_H17/T_H22 immune polarization of AD and psoriasis, respectively. Upregulated MF genes were involved in immune checkpoint regulation *(CTLA4, ICOS),* lymphoid trafficking *(CCR7, CCR8),* antigen presentation *(HLA-DRA, LAMP3),* T-cell survival *(TNFSF13B, BIRC3),* metabolism *(BCAT1, ENPP4, LIPA),* and cell structure and homeostasis *(CLIC2, DOCK10, EPB41L3, MCOLN2, MS4A14, S100B).* We identified a 5-marker gene classifier (including *IL36A*) that accurately distinguished MF from both AD and psoriasis, which was validated in an independent dataset.

Conclusions: By capturing MF-specific signatures that are distinct from AD and psoriasis, tape stripping has the potential to serve as a diagnostic tool to help differentiate MF from its nonmalignant mimickers. (J Allergy Clin Immunol 2026;■■■:■■■-■■■.)

Key words: *Cutaneous T-cell lymphoma, atopic dermatitis, psoriasis, tape stripping, transcriptomics, immune biomarkers, skin barrier*

Primary cutaneous T-cell lymphomas (CTCL) are a heterogeneous group of non-Hodgkin lymphomas,[1,2] of which mycosis fungoides (MF) is the most frequent entity.[3] Most cases present as indolent, early-stage disease (stages IA-IIA) that are characterized by patches and plaques, but approximately 25% develop into more aggressive, advanced-stage disease (stages IIB-IVB), clinically characterized by tumors and/or erythroderma and an overall 5-year survival rate of only 55% to 70%.[2-5] Importantly, clinical features of early-stage MF are often nonspecific and can be misclassified as benign chronic inflammatory skin diseases such as atopic dermatitis (AD) or psoriasis.[6,7] For this reason, it takes a median of 3 years from the first appearance of a skin lesion until a correct diagnosis is made.[7] Histopathology is a cornerstone of MF diagnosis, but results can be nonspecific, often necessitating multiple repeat biopsies.[8,9] This diagnostic delay highlights the need for better sampling approaches. On an immunologic level, early-stage MF generally shows a T_H1-dominant phenotype, whereas advanced stages shift more toward a T_H2 bias[10-13]—an immune axis that is also characteristically found in AD.[14] Psoriasis, in contrast, is dominated by T_H17 signaling pathways.[15-17] So far, these biomarkers are not available for routine testing, and no reliable diagnostic classifier exists.[10,12,18,19]

While full-thickness skin biopsy samples remain the reference standard for molecular skin investigations, tape stripping has emerged as a useful alternative.[20] This minimally invasive procedure, which bears no risk of pain, scarring, infection, or bleeding, can capture various disease markers at high sensitivity and specificity.[21-23] This approach has been utilized in AD, chronic hand eczema, psoriasis, seborrheic dermatitis, and hidradenitis suppurativa; however, data on the use of tape stripping in CTCL, including MF, remain limited, with a lack of comparisons to other diseases.[22,24-28] Techner et al[27] used a proteomic multiplex assay with a predefined, limited panel of established markers to distinguish CTCL from healthy control (HC) skin, and Qureshi et al[26] used mass spectrometry to distinguish lesional from nonlesional MF. Investigations comparing CTCL with benign inflammatory dermatoses have relied on targeted RNA expression profiling of skin biopsy samples rather than tape strips.[29,30] Thus, no transcriptomic study has been conducted using tape strips to differentiate CTCL from benign inflammatory skin diseases. To address this gap, we performed bulk RNA sequencing of skin tape strips to characterize the molecular signatures of MF, AD, psoriasis, and HC from both lesional and anatomically matched nonlesional skin (NL).

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Abbreviations used
AD: Atopic dermatitis
AUC: Area under the receiver operating characteristic curve
CPM: Counts per million
CTCL: Cutaneous T-cell lymphoma
DEG: Differentially expressed gene
EASI: Eczema Area and Severity Index
HC: Healthy control
IGA/PGA: Investigator's Global Assessment/Physician's Global Assessment
LOOCV: Leave-one-out cross-validated
MF: Mycosis fungoides
NL: Nonlesional skin
P-NRS: Pruritus Numerical Rating Scale

METHODS

Study population and data collection

The study included 116 participants: 36 with AD, 32 with psoriasis, 18 with MF, and 30 HCs (Table I). A total of 88.9% of patients with MF had early-stage disease (Table II). All individuals were recruited from the outpatient clinic of the Department of Dermatology at the Icahn School of Medicine at Mount Sinai, and diagnoses were confirmed by board-certified dermatologists on the basis of clinical evaluation and, where appropriate, histopathologic and/or laboratory confirmation. HCs were volunteers without a history of inflammatory skin disease or active malignancy. Lesional MF, AD, and psoriasis sampling was restricted to the most representative trunk and extremity skin alongside anatomically matched nonlesional sites. Prior and concomitant treatments in patients with MF are listed in Table II. AD and psoriasis participants were free of systemic immunomodulatory therapy, systemic corticosteroids, and topically directed treatments at the time of sampling. All 4 groups were matched for age, sex, and body location (trunk and extremities). Before inclusion in the study, participants were provided with a written informed consent form with information about a research protocol approved by the local Institutional Review Board. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Clinical and demographic data were obtained at the time of study enrollment through patient interviews and chart review. Age, sex, and self-reported race/ethnicity were recorded for all participants. AD severity was captured by the Investigator's Global Assessment/Physician's Global Assessment (IGA/PGA), Eczema Area and Severity Index (EASI), and Pruritus Numerical Rating Scale (P-NRS) instruments; psoriasis severity was assessed by IGA/PGA. CTCL disease stage was assessed by the Mycosis Fungoides Group classification and staging system revised by the International Society for Cutaneous Lymphomas and the European Organization of Research and Treatment of Cancer.[31] When necessary for diagnostic confirmation, additional clinical information, including laboratory values or pathology results, was obtained from the electronic medical record.

Tape-strip acquisition

For each participant, 20 consecutive tape strips (D-Squame; CuDerm, Dallas, Tex) were taken from at least one lesional CTCL, AD, psoriasis, or healthy skin area at the most representative anatomic site. Tape strips from adjacent NL were also collected in patients from each disease group. Tape strips were applied to the skin surface with uniform pressure for approximately 5 seconds with a D500 D-Squame pressure instrument. After collection, the tapes were transferred to storage cards and then maintained at −80°C until processing.

RNA extraction and sequencing

Total RNA was extracted from tape strips with the miRNeasy Mini Kit (Qiagen, Hilden, Germany) following the supplier's protocol. RNA yield and integrity were verified with a TapeStation 4200 system (Agilent Technologies, Santa Clara, Calif). Libraries for sequencing were prepared with the Ion AmpliSeq Transcriptome Human Gene Expression Kit (Thermo Fisher Scientific, Waltham, Mass). After quantification, libraries were normalized, pooled, and sequenced on Ion S550 chips with the Ion S5 XL platform (Thermo Fisher Scientific) to generate transcriptome-wide profiles.

Statistical and bioinformatic analyses

Bioinformatic and statistical analyses were carried out by R and RStudio software with Bioconductor packages. Read quality was evaluated with 'FastQC' and 'MultiQC', and alignment to the human reference genomewas performed with 'STAR'.[32] Gene-level counts were assigned with 'featureCounts,' and transcripts expressed at very low levels were excluded before normalization.

Expression values were transformed with 'voom,'[33] incorporating quantile normalization and precision weights. Linear modeling was implemented with the 'limma' package,[34] adjusting for batch effects, and significance was determined by moderated *t* statistics. *P* values were corrected for multiple testing with the Benjamini-Hochberg procedure, and transcripts were considered differentially expressed when absolute fold change exceeded 2 and false discovery rate was below 0.05.

Gene set enrichment was investigated by the gene set variation analysis approach. Enrichment analysis was conducted using annotations derived from the Reactome database via EnrichR.[35,36] Group-level comparisons of demographic or clinical variables were conducted for categorical outcomes by chi-square test or Fisher exact test, as appropriate according to expected counts, and Kruskal-Wallis test was used for continuous outcomes.

CTCL classifier development

We fit 3 multiple logistic regression models: (1) a model to discriminate CTCL from AD, (2) a model to discriminate CTCL from psoriasis, and (3) a model to discriminate CTCL from both AD and psoriasis. Instead of analyzing the entire transcriptome, we explored a subset of immune-related genes curated in our lab, including the panels discussed in Esaki et al[37] and Werfel et al.[38] This targeted approach constrained the stochastic feature selection process to genes with established immunologic relevance, thereby enhancing the biological interpretability and reducing dimensionality in subsequent analyses.

Because of the sample size, model fitting was not performed with the training-test paradigm. Instead, a stochastic search algorithm was used to navigate the model space and select the optimal subset of immune genes that best discriminated CTCL from other skin conditions. We tested models with 3, 4, and 5 genes and found that 5-gene models had the best performance;

TABLE I. Demographic characteristics

Characteristic	AD	Psoriasis	CTCL	HC	*P* value
No. patients	36	32	18	30	
Age (years), mean ± SD	49.8 ± 15.8	45.7 ± 13.6	51.7 ± 15.8	44.6 ± 13.7	.35
Sex (M/F)	22/14	20/12	10/8	18/12	.97
Race/ethnicity, n (%)					<.001
White	20 (55.6)	29 (90.6)	9 (50.0)	20 (66.7)	
Black or African American	6 (16.7)	0	3 (16.7)	8 (26.7)	
Asian	6 (16.7)	3 (9.4)	2 (11.1)	2 (6.7)	
Other	3 (8.3)	0	4 (22.2)	0	
Not reported	1 (2.8)	0	0	0	
Severity scores					
IGA/PGA, n (%)					
2	3 (8.3)	4 (13)	NA	NA	
3	21 (58)	23 (72)	NA	NA	
4	11 (31)	5 (16)	NA	NA	
Not reported	1 (2.8)	0	NA	NA	
EASI, mean (range)	22.4 (1.4-63.6)	NA	NA	NA	
P-NRS, mean (range)	6.8 (1-10)	3.6 (0-9)	NA	NA	

Data are presented as nos. (%) unless otherwise indicated.
NA, Not applicable.

adding more genes did not improve it. Subsequently, genetic algorithms were used to select the set of 5 genes that best discriminated CTCL from other skin conditions. The selection was based on the area under the receiver operating characteristic curve (AUC), the Akaike Information Criterion, and the significance of the coefficients in the model to ensure that the selected genes were meaningful predictors of CTCL. To account for multicollinearity among genes, we estimated the coefficients of the logistic regression models with a ridge regression approach. The optimal value of the regularization parameter was determined through cross-validation to balance model complexity and predictive accuracy. The performance of the final models was evaluated by AUC, sensitivity, specificity, and accuracy metrics. We used bootstrap techniques for evaluating the confidence intervals for the AUC. The selected gene sets were further analyzed for their biological relevance to CTCL pathogenesis and potential as diagnostic biomarkers.

Validation of 5-marker classifiers discriminating CTCL from AD and psoriasis

To mitigate overfitting, the stochastic search was coupled with a multicriteria evaluation of the model's performance. This evaluation consisted of estimating the AUC by bootstrapping the sample, minimizing the Akaike Information Criterion, and assessing the significance of markers in the logistic regression. As an additional evaluation, we validated the selected markers and the use of ridge logistic regression to discriminate CTCL from AD and psoriasis in an external dataset.

Public skin-transcriptome datasets were retrieved from the National Center for Biotechnology Information Gene Expression Omnibus (www.ncbi.nlm.nih.gov/geo) and processed with a single reproducible pipeline.[39,40] Because no public bulk series contains CTCL together with these dermatoses, the positive and comparator groups were drawn from independent RNA sequencing cohorts: CTCL was represented by lesional MF skin samples from advanced-stage disease (GSE168508; n = 49) and the comparators by lesional AD (GSE121212; n = 21) and lesional psoriasis (GSE121212; n = 28). Each study's healthy/uninvolved skin served as an internal reference. Controls for GSE168508 were anchored to 1420 GTEx samples from healthy skin. Expression was placed on a common log-CPM scale: $\log_2(\text{CPM} + 1)$(GSE168508 was already provided in CPM and the GSE121212 raw counts were CPM-normalized to match). To mitigate cross-study batch effects, every marker was then expressed as a z score relative to its own study's HCs. For each panel, a binary logistic regression model (CTCL = positive) was fit, and discrimination was assessed by leave-one-out cross-validated (LOOCV) AUC, with sensitivity and specificity evaluated at a probability threshold of 0.5.

RESULTS

Study cohort

The study enrolled and collected tape strips from 116 participants, including 36 with AD, 32 with psoriasis, 18 with CTCL, specifically MF, and 30 HCs (Table I). The mean age was comparable across groups (mean age range across groups, 44.6-51.7 years, $P = .4$), and sex distribution did not differ significantly ($P = .97$). Racial and ethnic composition varied between cohorts ($P = .0016$), with a higher proportion of White participants in the psoriasis group and greater representation of Black or African American individuals in the CTCL and HC cohorts. Disease severity scores reflected moderate to severe disease in the inflammatory cohorts. Disease severity in the inflammatory cohorts was predominantly moderate; 58% of AD and 72% of psoriasis participants scored an IGA/PGA of 3 (moderate), while 31% and 16%, respectively, scored a 4 (severe). Additionally, AD participants demonstrated a mean EASI of 22.4 and a high itch burden, with a mean P-NRS of 6.8. In the CTCL group, the majority of patients (88.9%) had early-stage MF (stages IA-IIA) (Table II), representing the population in which diagnostic overlap with benign inflammatory dermatoses is most common.[30]

Tape-strip transcriptomics of CTCL compared to AD, psoriasis, and HC skin

Principal component analysis of normalized transcriptomic profiles revealed distinct clustering patterns of lesional AD, psoriasis, and CTCL compared to HC (Fig 1, *A*). Across all

TABLE II. Individual CTCL patient characteristics

Patient ID	Age (years)	Sex	Diagnosis	CTCL disease stage	Fitzpatrick skin type	Type of lesion sampled	Anatomic location of lesional sample	Concomitant treatment at time of sample collection	Prior treatments	Disease duration
1	27	M	MF	IA	III	Plaque	Trunk	NB-UVB	Clobetasol 0.05% ointment, triamcinolone 0.1% ointment	4 months
2	29	F	MF	IA	V	Plaque	Left breast	NB-UVB, triamcinolone 0.1% ointment, hydrocortisone 2.5% cream, tacrolimus 0.1% ointment	Betamethasone 0.05% ointment	11 months
3	38	F	MF	IA	VI	Patch	Left posterior shoulder	None	Triamcinolone 0.1% cream	1 year
4	51	M	MF	IA	III	Patch	Right lateral upper arm	Ritlecitinib 200 mg once daily	NB-UVB, triamcinolone 0.1% ointment, desoximetasone 0.05% gel	2 years
5	57	F	MF	IA	IV	Plaque	Right inner elbow	NB-UVB	None	13 years
6	60	F	MF	IA	II	Patch	Abdomen	None	NB-UVB, triamcinolone 0.1% cream, hydrocortisone 2.5% cream	3 years
7	62	F	MF	IA	IV	Patch	Left upper back	NB-UVB	PUVA	7 years
8	66	F	MF	IA	II	Patch	Right lower abdominal quadrant	NB-UVB	Hydrocortisone 2.5% ointment, tacrolimus 0.1% ointment	7 years
9	73	M	MF	IA	V	Patch	Right inferior flank	NB-UVB, triamcinolone 0.1% ointment	None	22 years
10	33	M	MF	IB	IV	Patch	Right thigh	NB-UVB	PUVA	9 years
11	36	M	MF	IB	II	Plaque	Medial right dorsal foot	NB-UVB	NB-UVB, triamcinolone 0.1% ointment	3 years
12	47	F	MF	IB	V	Patch	Right scapula	NB-UVB, triamcinolone 0.1% ointment	None	3 years
13	55	M	MF	IB	I	Patch	Right lower back	None	Triamcinolone 0.1% cream	3 months
14	65	M	MF	IB	IV	NA	Left upper back	NA	NA	NA
15	65	F	MF	IB	IV	Plaque	Left lateral abdomen	Triamcinolone 0.1% cream	Peginterferon alfa-2a 180 μg once weekly, NB-UVB, halobetasol propionate 0.05% cream	3 years
16	77	M	MF	IB	IV	Patch	Right chest	Acitretin 25 mg once daily, prednisone 10 mg once daily, NB-UVB, triamcinolone 0.1% ointment	Halobetasol propionate 0.05% ointment	1 year
17	58	M	MF	IIB	II	Plaque	Left leg	Bexarotene 450 mg once daily, NB-UVB	Bexarotene 150 mg once daily	2 years
18	31	M	MF	IIIA	IV	Plaque	Right lateral abdomen	None	Methotrexate 2.5 mg once weekly, prednisone 10 mg once daily, NB-UVB, ILTAC, triamcinolone 0.1% ointment	10 years

ILTAC, Intralesional triamcinolone acetonide; *NA,* not applicable; *NB-UVB,* narrow-band ultraviolet B therapy; *PUVA,* psoralen and ultraviolet A.

cohorts, nonlesional samples displayed greater transcriptional heterogeneity than lesional samples, consistent with variable subclinical immune activation. In AD, lesional and nonlesional samples clustered with substantial overlap, indicating widespread transcriptional dysregulation that extends well beyond clinically involved skin, in line with previous reports.[22,41,42] In contrast, nonlesional psoriasis and CTCL were more clearly separated from their respective lesional counterparts, largely overlapping with HC samples (Fig 1, *A*). These patterns suggest that subclinical molecular alterations in clinically uninvolved skin are most pronounced in AD, whereas they appear much more limited in psoriasis and CTCL. When calculating differentially expressed genes (DEGs) between AD, psoriasis, and CTCL compared to HC skin, we found both unique and shared genes between diagnoses, with a greater overlap between psoriasis and AD than either with CTCL, as depicted in the Venn diagram comprising Fig 1, *B*. In line with the principal component analysis, differences between lesional and nonlesional skin were lowest in AD, but comparable between psoriasis and CTCL (Fig 1, *C*). Consistently, the number of shared up- and downregulated genes between psoriasis and CTCL exceeded those shared between AD and either condition, likely reflecting the relatively few DEGs between lesional and nonlesional AD (Fig 1, *C*). Taken together, calculation of overall transcriptomic alterations in relation to HC skin revealed a higher degree of dysregulation in lesional than in nonlesional tissues in all cohorts (Fig 1, *D*).

Top dysregulated transcripts in CTCL samples

We next assessed the top up- and downregulated DEGs in both lesional and nonlesional CTCL compared to all other groups (Fig 2, *A* and *B,* and see Fig E1 in the Online Repository available at www.jacionline.org). As revealed in a heat map, mean DEG expression levels in nonlesional AD were generally higher than in nonlesional psoriasis or HC skin, whereas nonlesional CTCL showed closest similarities with HC (Fig 2, *A* and *B,* and Fig E1, *A* and *B*). Most genes upregulated in lesional CTCL were also upregulated in lesional AD and psoriasis compared to HC alone (Fig 2, *A,* and Fig E1, *A*). Psoriasis showed highest levels of T_H1 *(CXCL9)*-,[43] T_H1/T_H17 *(IL12B)*-,[44] and T_H17 *(DEFB4A)*-associated mediators,[45] whereas both lesional AD and CTCL exhibited similarly low expression of these psoriasis-associated genes (Fig 2, *A,* and Fig E1, *A*). The highest DEG levels in lesional CTCL included genes involved in

checkpoint regulation and costimulatory signaling,[46,47] including *CTLA4* and *ICOS* (Fig 2, *A,* and Fig E1, *A*). *TIGIT,* another immune checkpoint inhibitor previously reported to be upregulated in CTCL,[48,49] was also increased in CTCL lesions within our dataset (Fig 2, *A,* and Fig E1, *A*). We additionally observed high expression of the α_2-macroglobulin gene *A2M,* a regulator of cytokine activity,[50] as well as chemokine receptors mediating skin homing and lymphoid trafficking, namely *CCR8* and *CCR7*,[51,52] in lesional CTCL (Fig 2, *A,* and Fig E1, *A*). Lesional CTCL samples also showed elevated levels of *HLA-DRA, HLA-DQA2,* and *LAMP3* (Fig 2, *A,* and Fig E1, *A*), which may point to enhanced antigen presentation and dendritic cell activation.[46,53-56] We also found CTCL-associated upregulation of the immune-activation receptor *SLAMF7,*[57] the G protein-coupled receptor signaling regulators *RGS1* and *RAMP1,*[58] as well as lymphocyte survival promoters such as *TNFSF13B* (BAFF) and *BIRC3,*[59,60] which might be associated with sustained T-cell activation and proliferation facilitated by the lesional CTCL microenvironment. Beyond transcripts involved in immune signaling, CTCL lesions showed elevated expression of metabolic regulators *(BCAT1, ENPP4, LIPA),*[61-63] markers of cytoskeletal structure and organization *(EPB41L3, DOCK10),*[64,65] and ion transport and homeostasis *(MCOLN2, CLIC2, S100B, MS4A14)*[66-70] that were higher than in all other groups investigated (Fig 2, *A,* and Fig E1, *A*).

When assessing the top downregulated DEGs in CTCL compared with all other groups, the majority were reduced only relative to genes upregulated in lesional AD and psoriasis; only a few genes were significantly reduced in relation to HC samples (Fig 2, *B,* and Fig E1, *B*). In lesional AD, we found characteristic upregulation of the paradigmatic T_H2 cytokine gene *IL13* driving atopic inflammation and tissue remodeling,[14,71] which was entirely absent in CTCL (Fig 2, *B,* and Fig E1, *B*). Additional genes with highest mean expression in lesional AD included *MMP10,* which has been associated with skin barrier dysfunction,[72] and *CXCR1,* thought to contribute to enhanced T-cell migration to sites of inflammation (Fig 2, *B,* and Fig E1, *B*).[73] In psoriasis lesions, upregulated transcripts were dominated by established T_H17–associated mediators, including *IL17A* and *IL17F,*[74] which again were not observed in CTCL (Fig 2, *B,* and Fig E1, *B*). Other upregulated genes in lesional psoriasis included those involved in immune regulation and proinflammatory response *(IFIT1, ZBP1, GBP5, RSAD2, FCGR1A, C3AR1, IL36A, ORM1, VNN1, TCN1, RHCG, TMPRSS11D).*[75-86]

Among markers that were downregulated in lesional CTCL compared to HC, we detected *IL17C,* which encodes a keratinocyte-derived cytokine involved in inflammation and antimicrobial defense,[87,88] which was also decreased compared to lesional AD and psoriasis (Fig 2, *B,* and Fig E1, *B*). Similarly, *OPRPN,* which encodes opiorphin prepropeptide, an endogenous opioid modulator, had the lowest mean expression in CTCL lesions, potentially suggesting altered pain sensation pathways.[89] *GSC* (goosecoid), a transcription factor involved in epithelial differentiation,[90] was also among the most strongly suppressed transcripts in CTCL lesions compared to all other groups (Fig 2, *B,* and Fig E1, *B*). Overall, transcriptomic patterns reflect the polarized T_H2 and T_H17 programs that define AD and psoriasis, respectively, that were not found in lesional CTCL.

Immune gene profiling reveals T-cell activation and checkpoint dysregulation in lesional CTCL

We next examined the specific expression of immune-related transcripts to identify features that distinguish our CTCL samples from HC and inflammatory dermatoses (Fig 3, and see Fig E2 in the Online Repository available at www.jacionline.org). Compared with HC, both lesional and nonlesional AD tape strips demonstrated broad immune activation of type 2 and type 22 immunity, namely *IL19, IL20, IL22, IL31, CCL18,* and *CCL24,*[91,92] in line with previous reports.[93,94] In psoriasis, we found further upregulation of immune trafficking and $T_H17/22$-associated genes including *IL22, CXCL1, CXCL8,* and *S100A12,*[95-97] the gene encoding the general inflammation marker IL-6, and the tissue homing and retention associated genes, *CD69* and *CXCR4* (Fig 3, Fig E2).[98-100] Lesional CTCL revealed marked expression of genes involved in T-cell activation, antigen presentation, and costimulation, including *CD2, CD83, CD86,* and *CD1A*.[101-104] We also observed increased expression of the matrix remodeling metalloproteinase gene *MMP12* in lesional CTCL compared with both HC and NL. Besides its general inflammatory properties,[23] MMP12 plays a role in the degradation of collagen IV and other basement membrane components, potentially facilitating the typical epidermotropism of malignant T cells.[105-107] Other genes significantly upregulated in lesional CTCL included several encoding proinflammatory chemokines and chemokine receptors *(CCL3, CCL18),*[29,30,108] T-cell receptor components *(CD3D, CD3E, CD3G),*[109] and *ITK*, encoding the IL-2–inducible T-cell kinase.[110] While these genes were upregulated in lesional CTCL compared to HC skin, their expression did not differ significantly from lesional AD or psoriasis. A few transcripts, however, did distinguish malignant from benign inflammatory diseases. Notably, *ITGAX,* which encodes a dendritic cell–associated integrin,[111] was strongly elevated in AD but was only slightly increased in CTCL compared to HC skin. Similarly, *CD2* and *CD1A* were upregulated in both CTCL and psoriasis compared to HC, but to a much greater degree in CTCL. Several mediators that were strongly upregulated in psoriasis, including *IL3, IL6, CCL3, CCL19, CCL24,* and *CXCL8,* were absent or attenuated in CTCL, emphasizing distinct marker expression of benign and malignant inflammation.

CTCL demonstrates mixed immune activation and barrier impairment

Pathway-level analyses confirmed elevated immune gene expression in lesional skin of AD, psoriasis, and CTCL, as well as in nonlesional AD (Fig 4, *A*). Conversely, decreases in epidermal differentiation complex and cornified envelope markers, surrogates for the overall integrity of the epidermal barrier, were visible in both lesional CTCL and lesional AD skin, although with a bimodal distribution in the latter (Fig 4, *B*), reinforcing the known disease heterogeneity in AD.[14] T_H1 activation was significantly higher in lesional versus nonlesional CTCL skin (Fig 4, *C*), while the highest levels of T_H2 activation were observed in AD, with upregulation in both lesional skin and NL (Fig 4, *D*). Lesional psoriasis showed the classic T_H17 and T_H22 upregulation (Fig 4, *E* and *F*).[15-17] CTCL lesions, in contrast, did not show a uniform immune activation pattern but rather a more complex and blended immune profile

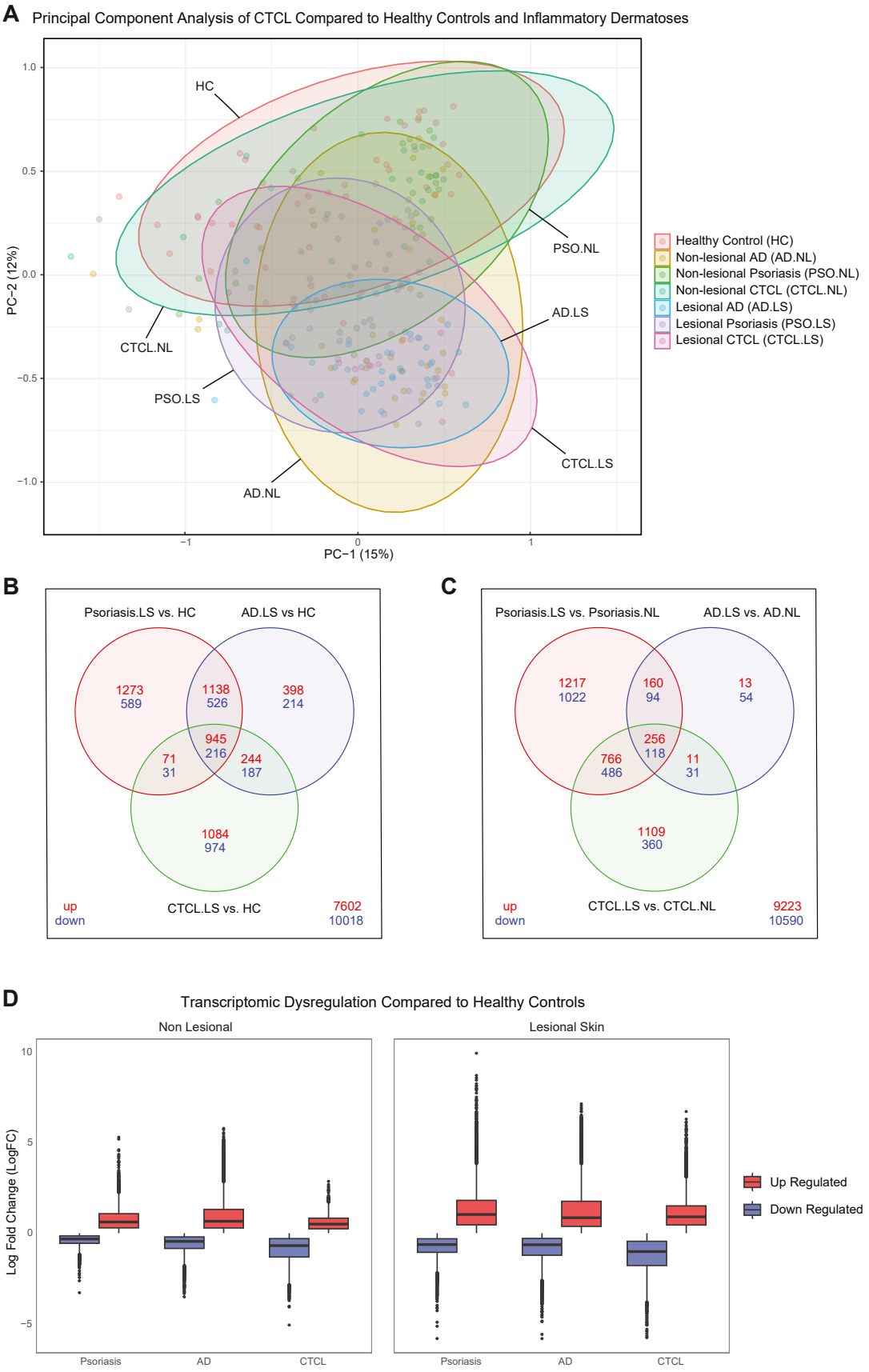


FIG 1. Overview of skin tape-strip transcriptome landscape in CTCL, AD, psoriasis, and HCs. **(A)** PCA of normalized transcriptomic data from tape strips collected from lesional skin and NL of patients with CTCL, AD, and psoriasis as well as from HC skin. Values in parentheses indicate the percentage of variance

(Fig 4, *A-F*). Both T_H1- and T_H2-associated gene sets were significantly elevated in lesional compared to nonlesional CTCL, but lesional T_H2 activation was lower in CTCL than in AD (Fig 4, *C* and *D*). T_H17 and T_H22 pathways were not as prominently increased in CTCL as in psoriasis, but they remained significantly upregulated in CTCL lesional skin compared to nonlesional or HC skin (Fig 4, *E* and *F*). These patterns suggest that CTCL lesions incorporate elements of multiple inflammatory pathways rather than conforming to a single polarized axis.

Classifier to distinguish lesional CTCL from AD and/or psoriasis

Given the mixed phenotype of CTCL lesions, we next calculated logistic regression classifiers to discriminate CTCL from AD and/or psoriasis by performing a stochastic search algorithm of immune genes, revealing best performance of three different 5-marker combinations that accurately differentiated CTCL from the inflammatory skin diseases (Fig 5). Best AUCs were obtained for lesional expression of *CCR1, CXCL9, IL36A, IL36RN,* and *STAT6* for CTCL versus AD, whereas *CAMP, CXCL14, IL17A, IL36A,* and *LAG3* best discriminated CTCL from psoriasis (Fig 5, *A* and *B*). When assessing lesional gene expression of CTCL versus both AD and psoriasis, we found the best performance with *CD3G, CXCL11, FCER1A, IL36A,* and *STAT6* (Fig 5, *C*). Corresponding smoothed receiver operating characteristic curves and AUC 95% confidence intervals for the multivariate logistic ridge regression showed nearly complete separation of CTCL from these benign inflammatory dermatoses across all 3 comparisons: CTCL vs AD (Fig 5, *D*), CTCL vs psoriasis (Fig 5, *E*), and CTCL vs AD and psoriasis (Fig 5, *F*).

We next tested our classifiers in two published skin biopsy–based transcriptomic datasets.[39,40] Both classifiers separated CTCL (ie, advanced-stage MF) from both benign conditions (Fig 5, *G* and *H*). The AD classifier achieved a LOOCV AUC of 0.896 (sensitivity = 0.96, specificity = 0.90) (Fig 5, *I*). The psoriasis classifier achieved a LOOCV AUC of 0.997 (sensitivity = 1, specificity = 0.93), with nearly complete separation between groups (Fig 5, *J*). Together, these results indicate that both 5-marker logistic regression classifiers discriminate CTCL from psoriasis and from AD with high cross-validated accuracy, supporting their potential utility in the molecular differential diagnosis of both early-stage and advanced-stage MF from benign inflammatory dermatoses.

DISCUSSION

Our study demonstrates the feasibility of minimally invasive tape stripping to capture the characteristic transcriptomic dysregulation and immune skewing found in lesional MF—not only compared to HC but also with the benign inflammatory mimickers AD and psoriasis. Genes previously described as increased in CTCL in biopsy-based transcriptomic studies, such as *BIRC3, CCL18, CCR7, CCR8, CD1A, CD2, CD3D, CD3E, CD3G, CD69, CD83, CD86, CTLA4, CXCR4, EPB41L3, HLA-DQA2, HLA-DRA, ICOS, ITK, LAMP3, MMP12, RGS1, S100B,* and *TIGIT,*[29,30,47-49,55,56,112-118] were recapitulated in our lesional MF tape-strip samples, highlighting the ability of epidermal sampling to capture key immune markers. Some transcripts that are often upregulated in lesional CTCL biopsy samples, including *TOX, STAT5A,* and *GNLY,*[27] were not detected at comparable levels in our samples, suggesting that upregulation of these transcripts may be limited to deeper dermal layers. Notably, our unbiased, transcriptome-wide approach demonstrated substantial concordance with a previous tape-strip biomarker study by Techner et al[27] that used a proteomic multiplex assay. Of the 24 primary markers highlighted in their targeted proteomic assay, 22 were sufficiently expressed for analysis. A majority of these evaluable transcripts (12 of 22) demonstrated significant differential expression, and some of the biomarkers they identified, such as cystatin-B *(CSTB)* and heme oxygenase-1 *(HMOX1),* were also elevated in our dataset, but fell just below our significance thresholds. This high degree of overlap is particularly striking given the differences in platform and scope: Techner et al evaluated 183 proteins, whereas our assessment of approximately 12,000 genes necessitated a rigorous correction for multiple comparisons.

In addition to validating biopsy-based transcriptomic studies, our analysis identified novel CTCL-associated genes. Several transcripts that had increased expression in lesional CTCL compared to healthy skin, including *A2M, BCAT1, DOCK10, ENPP4, MCOLN2, SLAMF7, RAMP1,* and *TNFSF13B,* have been reported to be upregulated in leukemias and B-cell lymphomas,[61,65,119-125] but they have not been previously implicated in cutaneous T-cell malignancies. We also identified multiple highly expressed genes without prior associations with CTCL or other lymphomas, such as *CLIC2, LIPA,* and *MS4A14.* Among these, *LIPA* was significantly elevated relative to psoriasis, suggesting its potential as a discriminative marker between CTCL and benign inflammatory dermatoses. Separation of CTCL from AD may rely on the diminished expression of the prototypic AD marker genes, such as *IL13,*[71] or others found in our analyses, including *ITGAX, CXCR1,* or *MMP10.*[72,73,111] These findings highlight previously unrecognized molecular features of CTCL that may have noninvasive diagnostic relevance.

In exploring the diagnostic implications of these transcriptomic differences, our multivariable logistic regression classifiers support the feasibility of using tape-strip transcriptomic evaluation to accurately differentiate CTCL from common inflammatory mimickers. Our 5-marker classifiers obtained nearly perfect discrimination of CTCL from AD, psoriasis, and both benign

explained by each principal component. *Points* represent individual samples, color-coded by group, with *ellipses* denoting 95% confidence intervals for multivariate *t*-distribution. (**B** and **C**) Venn diagrams of DEG counts comparing psoriasis, AD, and CTCL lesional skin against HC skin *(B)* and NL *(C).* Significantly upregulated genes are shown in *red* and downregulated genes in *blue.* Intersection areas denote number of DEGs shared across comparisons. *Bottom right numbers* indicate number of genes not differentially expressed in any comparison. DEGs were defined as |FCH| > 2 and FDR < 0.05. **(D)** Box plots showing distribution of log fold changes for significantly upregulated *(red)* and downregulated *(blue)* genes in nonlesional and lesional skin from patients with psoriasis, AD, and CTCL. *Boxes* represent interquartile range, with median indicated by *horizontal line; whiskers* extend to 1.5 times interquartile range, and individual *dots* denote outliers. *FCH,* Fold change; *FDR,* false discovery rate; *LS,* lesional skin; *PCA,* principal component analysis; *PSO,* psoriasis.

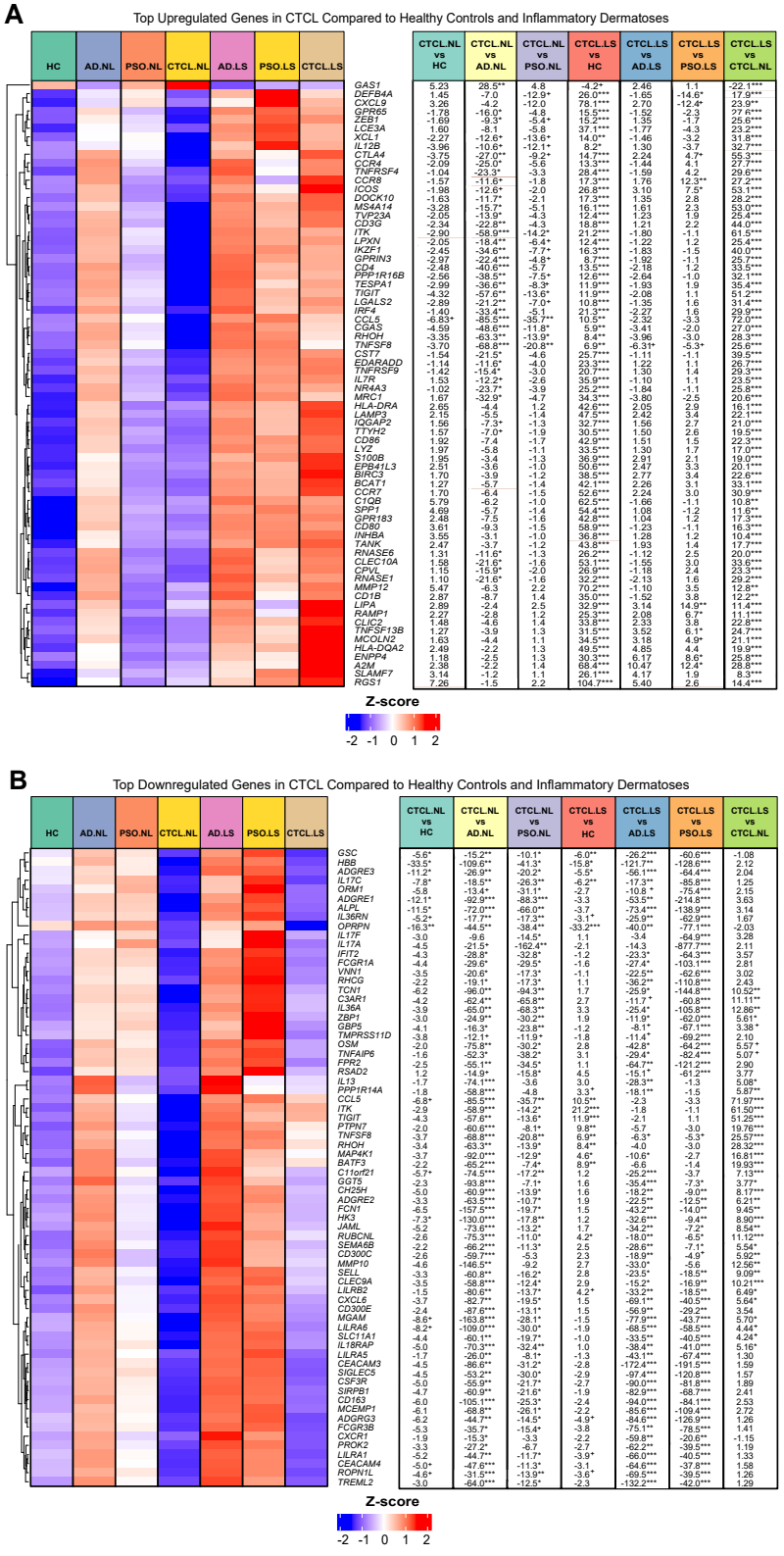
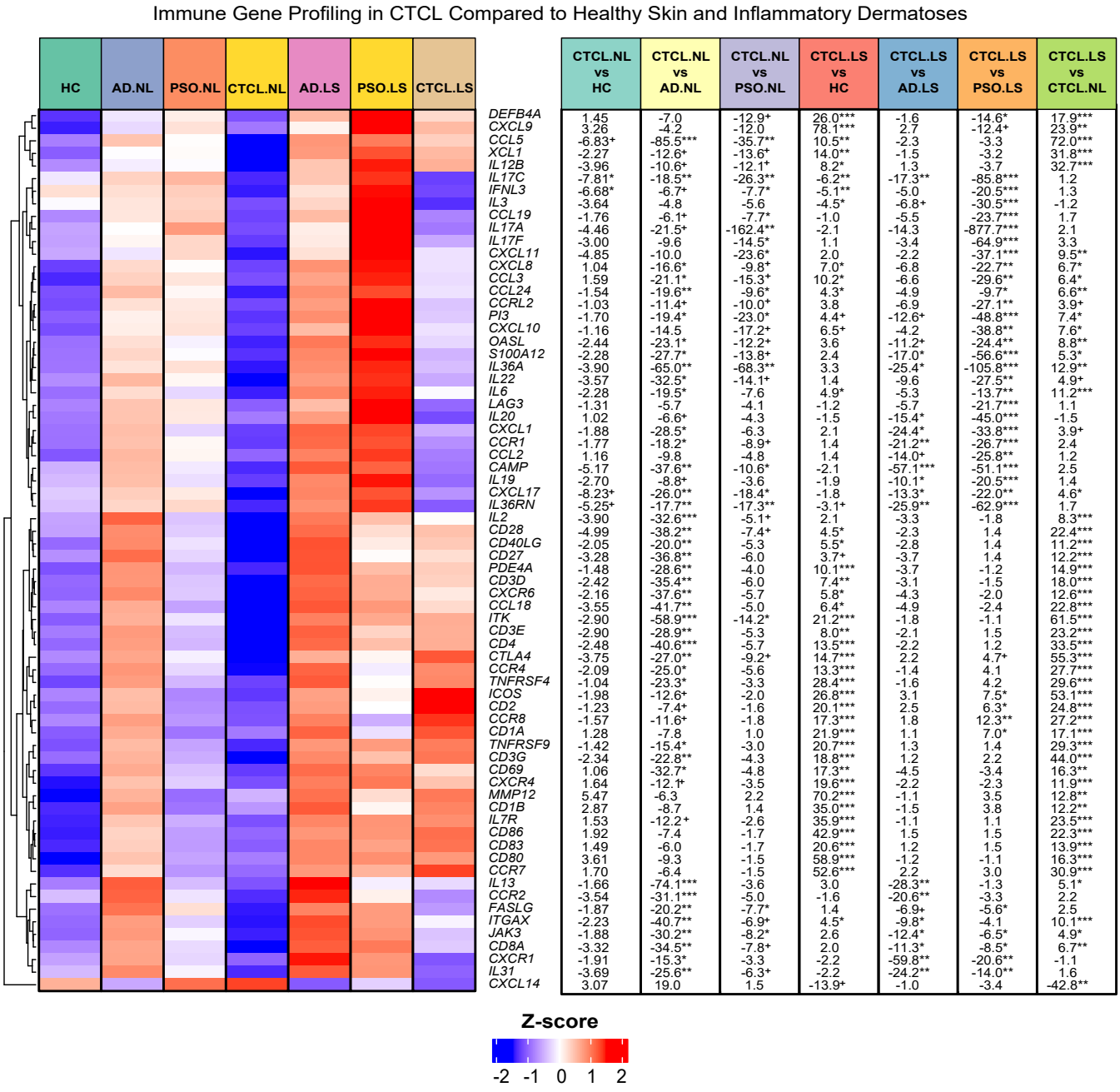


FIG 2. Global transcriptomic dysregulation in CTCL compared with AD, psoriasis, and HC skin. Heat maps depict top 70 **(A)** upregulated and **(B)** downregulated DEGs across all depicted group comparisons. Columns represent sample groups and rows represent individual genes, arranged by hierarchical clustering so that transcripts with similar expression patterns are displayed next to one another. Heat map colors reflect *z* scores of normalized expression levels, with *red* indicating higher expression and *blue* indicating lower expression relative to mean; color intensity corresponds to magnitude of deviation from mean. Numeric tables next to each heat map provide FCH values and significance levels for each comparison (|FCH| > 2, FDR < 0.05). $^{+}$FDR <0.1, *FDR < 0.05, **FDR < 0.01, ***FDR < 0.001. *FCH,* Fold change; *FDR,* false discovery rate; *LS,* lesional skin; *PSO,* psoriasis.



	CTCL.NL vs HC	CTCL.NL vs AD.NL	CTCL.NL vs PSO.NL	CTCL.LS vs HC	CTCL.LS vs AD.LS	CTCL.LS vs PSO.LS	CTCL.LS vs CTCL.NL
DEFB4A	1.45	-7.0	-12.9⁺	26.0***	-1.6	-14.6*	17.9***
CXCL9	3.26	-4.2	-12.0	78.1***	2.7	-12.4⁺	23.9**
CCL5	-6.83⁺	-85.5***	-35.7**	10.5**	-2.3	-3.3	72.0***
XCL1	-2.27	-12.6⁺	-13.6⁺	14.0**	-1.5	-3.2	31.8***
IL12B	-3.96	-10.6⁺	-12.1⁺	8.2*	1.3	-3.7	32.7***
IL17C	-7.81*	-18.5**	-26.3**	-6.2**	-17.3**	-85.8***	1.2
IFNL3	-6.68*	-6.7⁺	-7.7*	-5.1**	-5.0	-20.5***	1.3
IL3	-3.64	-4.8	-5.6	-4.5*	-6.8⁺	-30.5***	-1.2
CCL19	-1.76	-6.1⁺	-7.7*	-1.0	-5.5	-23.7***	1.7
IL17A	-4.46	-21.5⁺	-162.4**	-2.1	-14.3	-877.7***	2.1
IL17F	-3.00	-9.6	-14.5*	1.1	-3.4	-64.9***	3.3
CXCL11	-4.85	-10.0	-23.6*	2.0	-2.2	-37.1***	9.5**
CXCL8	1.04	-16.6*	-9.8*	7.0*	-6.8	-22.7**	6.7*
CCL3	1.59	-21.1*	-15.3*	10.2*	-6.6	-29.6**	6.4*
CCL24	-1.54	-19.6**	-9.6*	4.3*	-4.9	-9.7*	6.6**
CCRL2	-1.03	-11.4⁺	-10.0*	3.8	-6.9	-27.1**	3.9⁺
PI3	-1.70	-19.4*	-23.0*	4.4⁺	-12.6⁺	-48.8***	7.4*
CXCL10	-1.16	-14.5	-17.2⁺	6.5⁺	-4.2	-38.8**	7.6*
OASL	-2.44	-23.1*	-12.2⁺	3.6	-11.2⁺	-24.4**	8.8**
S100A12	-2.28	-27.7*	-13.8⁺	2.4	-17.0*	-56.6***	5.3*
IL36A	-3.90	-65.0**	-68.3**	3.3	-25.4*	-105.8***	12.9**
IL22	-3.57	-32.5*	-14.1⁺	1.4	-9.6	-27.5**	4.9⁺
IL6	-2.28	-19.5*	-7.6	4.9*	-5.3	-13.7**	11.2***
LAG3	-1.31	-5.7	-4.1	-1.2	-5.7	-21.7***	1.1
IL20	1.02	-6.6⁺	-4.3	-1.5	-15.4*	-45.0***	-1.5
CXCL1	-1.88	-28.5*	-6.3	2.1	-24.4*	-33.8***	3.9⁺
CCR1	-1.77	-18.2*	-8.9⁺	1.4	-21.2**	-26.7***	2.4
CCL2	1.16	-9.8	-4.8	1.4	-14.0⁺	-25.8**	1.2
CAMP	-5.17	-37.6**	-10.6*	-2.1	-57.1***	-51.1***	2.5
IL19	-2.70	-8.8⁺	-3.6	-1.9	-10.1*	-20.5***	1.4
CXCL17	-8.23⁺	-26.0**	-18.4*	-1.8	-13.3*	-22.0**	4.6*
IL36RN	-5.25⁺	-17.7**	-17.3**	-3.1⁺	-25.9**	-62.9***	1.7
IL2	-3.90	-32.6***	-5.1⁺	2.1	-3.3	-1.8	8.3***
CD28	-4.99	-38.2**	-7.4⁺	4.5*	-2.3	1.4	22.4***
CD40LG	-2.05	-20.0**	-5.3	5.5*	-2.8	1.4	11.2***
CD27	-3.28	-36.8**	-6.0	3.7⁺	-3.7	1.4	12.2***
PDE4A	-1.48	-28.6**	-4.0	10.1***	-3.7	-1.2	14.9***
CD3D	-2.42	-35.4**	-6.0	7.4**	-3.1	-1.5	18.0***
CXCR6	-2.16	-37.6**	-5.7	5.8*	-4.3	-2.0	12.6***
CCL18	-3.55	-41.7**	-5.0	6.4*	-4.9	-2.4	22.8***
ITK	-2.90	-58.9***	-14.2*	21.2***	-1.8	-1.1	61.5***
CD3E	-2.90	-28.9**	-5.3	8.0**	-2.1	1.5	23.2***
CD4	-2.48	-40.6***	-5.7	13.5***	-2.2	1.2	33.5***
CTLA4	-3.75	-27.0**	-9.2⁺	14.7***	2.2	4.7⁺	55.3***
CCR4	-2.09	-25.0*	-5.6	13.3***	-1.4	4.1	27.7***
TNFRSF4	-1.04	-23.3*	-3.3	28.4***	-1.6	4.2	29.6***
ICOS	-1.98	-12.6⁺	-2.0	26.8***	3.1	7.5*	53.1***
CD2	-1.23	-7.4⁺	-1.6	20.1***	2.5	6.3*	24.8***
CCR8	-1.57	-11.6⁺	-1.8	17.3***	1.8	12.3**	27.2***
CD1A	1.28	-7.8	1.0	21.9***	1.1	7.0*	17.1***
TNFRSF9	-1.42	-15.4*	-3.0	20.7***	1.3	1.4	29.3***
CD3G	-2.34	-22.8**	-4.3	18.8***	1.2	2.2	44.0***
CD69	1.06	-32.7*	-4.8	17.3**	-4.5	-3.4	16.3**
CXCR4	1.64	-12.1⁺	-3.5	19.6***	-2.2	-2.3	11.9***
MMP12	5.47	-6.3	2.2	70.2***	-1.1	3.5	12.8**
CD1B	2.87	-8.7	1.4	35.0***	-1.5	3.8	12.2**
IL7R	1.53	-12.2⁺	-2.6	35.9***	-1.1	1.1	23.5***
CD86	1.92	-7.4	-1.7	42.9***	1.5	1.5	22.3***
CD83	1.49	-6.0	-1.7	20.6***	1.2	1.5	13.9***
CD80	3.61	-9.3	-1.5	58.9***	-1.2	-1.1	16.3***
CCR7	1.70	-6.4	-1.5	52.6***	2.2	3.0	30.9***
IL13	-1.66	-74.1***	-3.6	3.0	-28.3**	-1.3	5.1*
CCR2	-3.54	-31.1***	-5.0	-1.6	-20.6**	-3.3	2.2
FASLG	-1.87	-20.2**	-7.7*	1.4	-6.9⁺	-5.6*	2.5
ITGAX	-2.23	-40.7**	-6.9⁺	4.5*	-9.8*	-4.1	10.1***
JAK3	-1.88	-30.2**	-8.2*	2.6	-12.4*	-6.5*	4.9*
CD8A	-3.32	-34.5**	-7.8⁺	2.0	-11.3*	-8.5*	6.7**
CXCR1	-1.91	-15.3*	-3.3	-2.2	-59.8**	-20.6**	-1.1
IL31	-3.69	-25.6**	-6.3⁺	-2.2	-24.2**	-14.0**	1.6
CXCL14	3.07	19.0	1.5	-13.9⁺	-1.0	-3.4	-42.8**

FIG 3. Mean expression of immune-related transcripts in CTCL, AD, psoriasis, and HC skin. Heat map of top 70 immune and pathway-associated genes significantly differentially expressed across cohorts in depicted comparisons. Columns represent sample groups and rows represent individual genes, which are arranged according to hierarchical clustering so that genes with similar expression patterns across samples are displayed next to each other. Heat map colors reflect *z* scores of normalized expression levels, with *red* indicating higher expression and *blue* indicating lower expression relative to mean; color intensity corresponds to magnitude of deviation from mean. Adjacent numeric table provides FCH values and significance levels for each comparison (|FCH| > 2 and FDR < 0.05). ⁺FDR <0.1, *FDR < 0.05, **FDR < 0.01, ***FDR < 0.001. *FCH,* Fold change; *FDR,* false discovery rate; *LS,* lesional skin; *PSO,* psoriasis.

conditions combined, suggesting that these limited transcript sets can detect disease-specific signatures using this noninvasive sampling approach. Thus, tape-strip transcriptomic testing may be a helpful adjunct to histopathologic evaluation, particularly in early-stage disease, where substantial clinical and pathologic overlap between CTCL and benign inflammatory dermatoses often contributes to diagnostic delay.[7,30]

Several limitations of our study warrant consideration. Prior studies have demonstrated that stratum corneum composition varies by anatomic site and can be influenced by topical

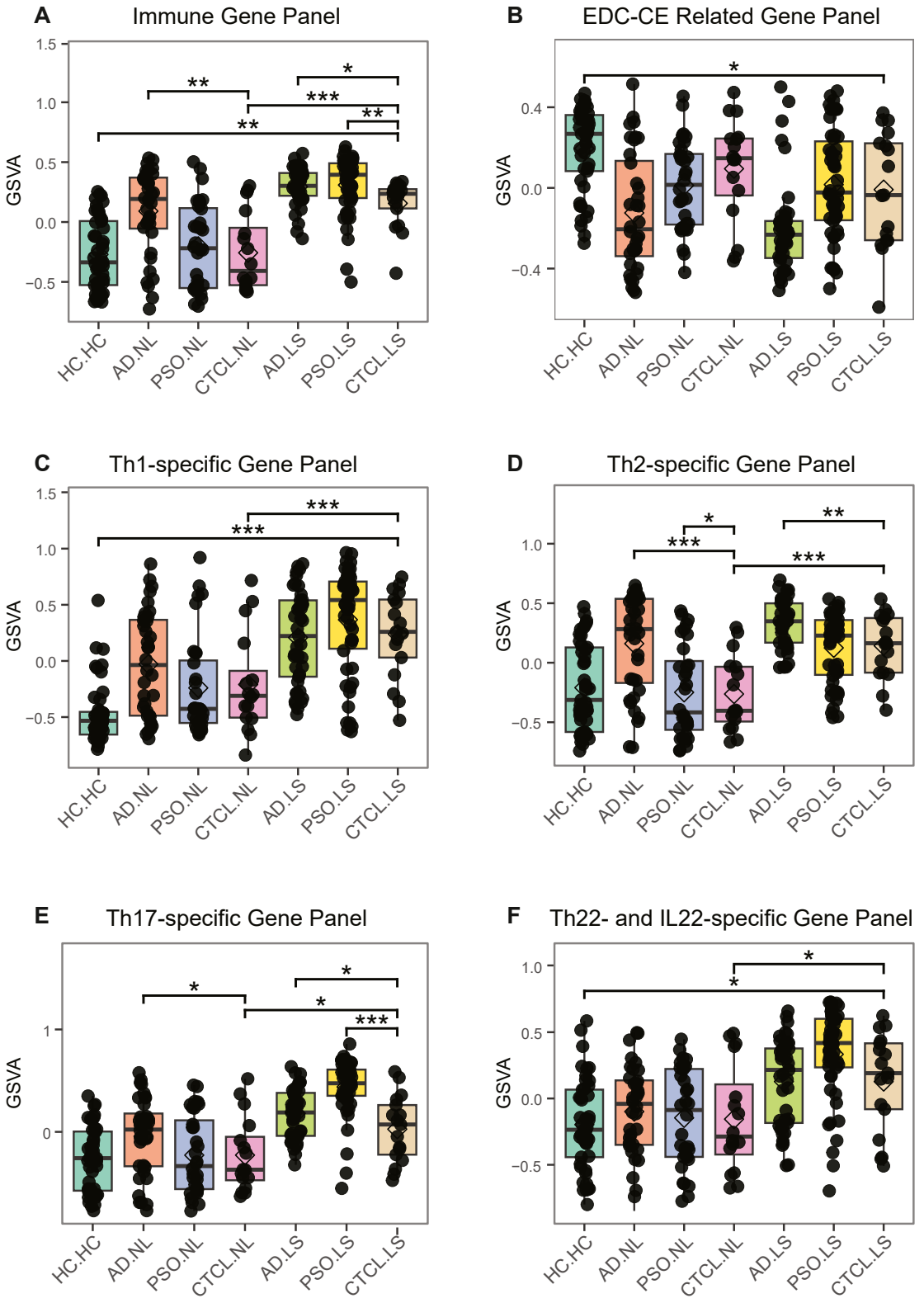


FIG 4. Pathway enrichment analyses of immune and barrier programs in CTCL, AD, psoriasis, and HC skin. GSVA and *z* score calculations were performed on normalized tape-strip transcriptomes to assess curated immune and epidermal barrier gene sets. **(A)** Expanded immune gene panel. **(B)** EDC and CE-related genes. **(C)** T_H1-specific gene set. **(D)** T_H2-specific gene set. **(E)** T_H17-specific gene set. **(F)** T_H22/IL-22–specific gene set. *Dots* represent individual samples; *diamonds,* group means; *horizontal lines,* medians; and *boxes,* interquartile ranges; *whiskers* extend to 1.5 times interquartile range. Statistical comparisons presented are those involving lesional or nonlesional CTCL samples. *FDR < 0.05, **FDR < 0.01, ***FDR < 0.001. *CE,* Cornified envelope; *EDC,* epidermal differentiation complex; *FDR,* false discovery rate; *GSVA,* gene set variation analysis; *LS,* lesional skin; *PSO,* psoriasis.

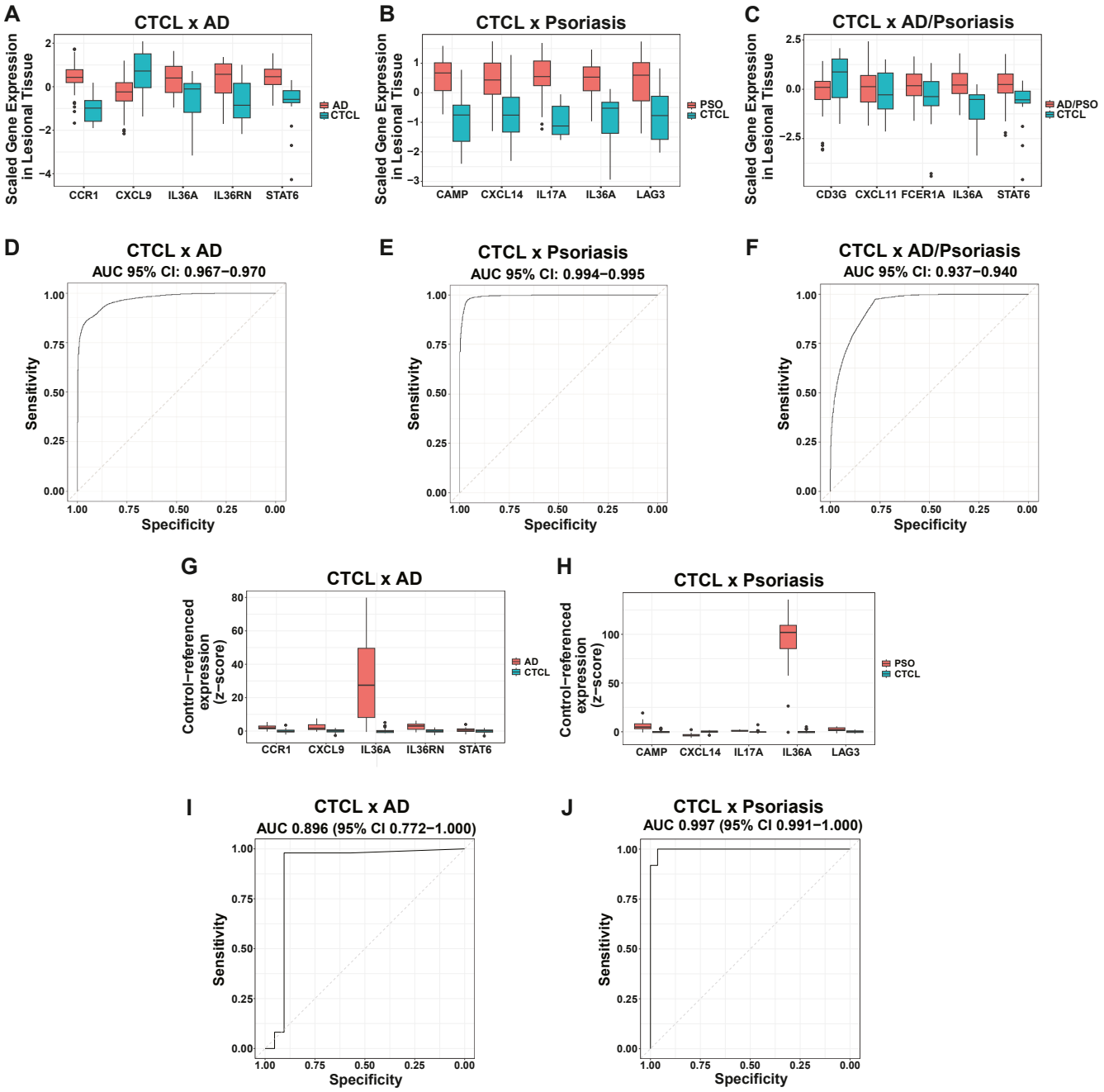


FIG 5. Summary of classification by 5 best-discriminating immune genes in CTCL vs AD, CTCL vs psoriasis, and CTCL vs AD and psoriasis selected by a stochastic search algorithm. **(A)** Box plots comparing lesional tape-strip expression between CTCL and AD for 5 selected genes *(CCR1, CXCL9, IL36A, IL36RN, STAT6).* **(B)** Box plots comparing lesional tape-strip expression between CTCL and psoriasis for 5 selected genes *(CAMP, CXCL14, IL17A, IL36A, LAG3).* **(C)** Box plots comparing lesional tape-strip expression between CTCL and AD or psoriasis for 5 selected genes *(CD3G, CXCL11, FCER1A, IL36A, STAT6).* **(D-F)** Smoothed ROC curves and AUC with 95% confidence intervals for multivariate logistic ridge regression that discriminates CTCL from benign inflammatory dermatoses. **(G-J)** Classifier validation using previously published advanced-stage MF, AD, and psoriasis bulk RNA-sequencing datasets from skin biopsy samples. *ROC,* Receiver operating characteristic.

therapies.[126] Because CTCL is a rare and clinically heterogeneous disease with variable lesion distribution,[127] we sampled the most clinically representative lesion at the time of the visit. While this resulting variability in anatomic site and treatment exposure is certainly a limitation, we collected nonlesional tape strips from sites immediately adjacent to the lesional samples to provide a within-patient control. Sampling was also restricted to the trunk and extremities, excluding regions such as the face, genitalia, and palms and soles, which exhibit significant differences in stratum corneum thickness and composition.[128,129]

Additionally, our benign inflammatory comparator cohorts primarily had moderate to severe disease, reflecting the population in which CTCL is most often considered in the differential diagnosis.[30,130] As a result, the ability of tape-strip transcriptomic profiling to distinguish mild AD or psoriasis from CTCL remains unclear. Furthermore, the CTCL cohort was mostly restricted to patch- and plaque-stage disease and was also heavily pretreated, consistent with a real-life cohort. Nonetheless, our classifiers were reproduced in an independent sample set of advanced-stage MF patients, suggesting relevance beyond patch and plaque lesions, and independent of concomitant treatment. Within the CTCL spectrum, we included only patients with classic MF, intentionally excluding patients with other clinical presentations, including folliculotrophic MF, because this variant is characterized by deeper perifollicular lymphocytic infiltrates, which might influence detection by tape strips.[131] As a result, these rare subsets of MF warrant investigation in future studies. Finally, our validation of the classifiers in published datasets has a few limitations. Because this validation is cross-study, disease class is partly confounded with cohort and batch effects, which control-referenced normalization mitigates but does not fully remove.

Overall, this approach to noninvasive transcriptomic profiling using tape strips captures the molecular environment of CTCL, reproducing established immune programs while discovering novel markers with diagnostic and therapeutic potential. Furthermore, in using this approach to compare CTCL to AD and psoriasis, we identified disease-specific transcripts that may help distinguish malignant from benign inflammatory skin disease. Importantly, the ability to detect distinct molecular signatures in early-stage MF, where clinical and histologic features often overlap with benign inflammatory dermatoses,[30] highlights the potential role of tape-strip profiling in improving diagnostic accuracy and reducing delays in care.

DISCLOSURE STATEMENT

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Disclosure of potential conflict of interest: A. Cices is an employee of Mount Sinai; has received personal fees from Veradermics, Galderma, Eli Lilly, Oruka, CeraVe, UCB, Sanofi, Apogee, Incyte, Novartis, LEO Pharma, Almirall, Botanix, Bristol Meyers Squibb, Fre Skincare, and Castle Biosciences; and is a clinical trial PI for LEO, Eli Lilly, Incyte, Johnson & Johnson, Moonlake, Novartis, Merck, and AbbVie. P. M. Brunner is an employee of Mount Sinai; has received personal fees from Almirall, Sanofi, Janssen, LEO Pharma, AbbVie, Pfizer, Boehringer Ingelheim, GSK, Regeneron, Eli Lilly, Celgene, Novartis, UCB, Merck, RAPT Therapeutics, Galderma, and BMS; and is a clinical trial PI for Pfizer, Nektar, UCB, and Abbvie. E. Guttman-Yassky is an employee of Mount Sinai; has received research grants (paid to institution) from Regeneron, Eli Lilly, Galderma, LEO Pharma, Pfizer, Amgen, GSK, Incyte, Sanofi, Bristol Meyers Squibb, Arcutis, AnaptysBio, Inmagene, AbbVie, Xencor, Q32 Bio, Opsidio, Apollo Therapeutics, Aclaris Therapeutics, Concerto Biosciences, Alumis, Apogee, Enveda, and Nektar; and has received personal fees from AbbVie, Aclaris Therapeutics, Almirall, Amgen, AnaptysBio, Apogee Therapeutics, Apollo Therapeutics, Arcutis, Artax Biopharma, Astria, Bambusa, Biolojic Design, Bionyra Pharma, Boerhinger Ingelheim, Bristol Meyers Squibb, Canyon Therapeutics, Celldex, Cue Biopharma, CytoReason, DBV, Dualitas Therapeutics, Electra Therapeutic, Eli Lilly, EMD Serono, Enveda Biosciences, Evommune, Galderma, Generate Biomedicines, Gilead Sciences, GSK, Infimmune, Inmagene, Janssen Biotech, Jasper Therapeutics, Kymera Therapeutics, LEO Pharma, Matchpoint Therapeutics, Merck, Navigator Medicines, Nektar Therapeutics, OpsidioLLC, Pfizer, Propeller Bio, Proteologix, Priovant Therapeutics, RAPT, RayThera, Recludix Pharma, Regeneron, Rubedo Life Sciences, Sanofi, SATO, Sitryx Therapeutics, SPARC, Takeda, Teva, Third Arc Bio (TAB), TRex Bio, Triveni Bio, UCB, Vellera Therapeutics, Ventyx, Veradermics, and VRG Therapeutics. The rest of the authors declare that they have no relevant conflicts of interest.

Clinical implication: Tape-strip transcriptomics is a noninvasive method to distinguish CTCL from AD and psoriasis, with a 5-gene classifier offering a potential diagnostic tool.

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