

Supplementary Online Content

Guttman-Yassky E, Diaz A, Pavel AB, et al. Use of tape strips to detect immune and barrier abnormalities in the skin of children with early-onset atopic dermatitis. *JAMA Dermatol*. Published October 9, 2019. doi:10.1001/jamadermatol.2019.2983

eMethods 1. Tape-Strip Collection

eMethods 2. RNA Extraction, Quality Control, and Quantitative Real-Time PCR

eMethods 3. Statistical Analysis

eTable 1. qRT-PCR Primers for 79 Immune and Barrier Mediators

eTable 2. Immunohistochemistry Antibodies

eTable 3. Summary of Past Tape-Strip Studies in Patients With Atopic Dermatitis

eTable 4. Means, Standard Errors, and Confidence Intervals for All Immune and Barrier Biomarkers

eFigure 1. Gene Expression of Inflammatory Biomarkers in Tape Strips

eFigure 2. Immune and Barrier AD Biomarkers Detected in Tape Strips

eFigure 3. Histology

eFigure 4. Expression of Biomarkers in Tape Strips Correlates With Clinical Severity

eFigure 5. Receiver Operating Characteristic Area Under the Curve (ROC AUC) in Tape Strips

eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods 1. Tape Strip Collection

Each large D-Squame (D102) tape-strip was applied to the antecubital fossa when possible for lesional skin and nearby skin was sampled for non-lesional. Tape-strips were applied with pressure with the Cu-derm pressurizer device (D500). The pressure instrument has a plunger mechanism to ensure even/consistent pressure is applied to each tape-strip. After pressure is applied and released, tape-strips are moved by gloved hands and stuck onto the D-Squame Standard storage cards (D120). Using a pen, small marks were made on the skin after placement of the first tape-strip to ensure consistent placement of each subsequent tape-strip. Cards were immediately stored on dry ice in biohazard specimen bags and then transferred to a -80°C freezer until time for shipment.

eMethods 2. RNA Extraction, Quality Control, and Quantitative Real-Time PCR

RNA was extracted for real-time polymerase chain reaction (RT-PCR) with the miRNAeasy Mini Kit (Qiagen, Hilden, Germany). Reverse transcription to complementary DNA (cDNA) from RNA was carried out using the High Capacity cDNA reverse transcription (Thermo fisher). TaqMan Low Density Array (TLDA) cards (Thermo fisher) were used for quantitative reverse transcription polymerase chain reaction (qRT-PCR). 500pg total RNA was used for PreAMP pool. Eukaryotic 18S recombinant RNA (rRNA) was used as an endogenous control. Expression values were normalized to *Rplp0*.

eMethods 3. Statistical Analysis

Threshold cycles [Ct] were normalized to *Rplp0* by negatively transforming the Ct values to $-dCt$. The undetected expression values were estimated for each gene as 20% of the minimum expression across all samples. Log₂-scale qRT-PCR expression data were modeled by a linear mixed effect model with biopsy type as a fixed effect and a random intercept for each patient. Means of each group were estimated using *lsmeans* and comparisons of interest were tested using contrast. Means and standard errors for each group and each marker are provided in eTable 4.

To evaluate the performance of an AD classifier we used Area Under the Receiver Operating Characteristic Curve (ROC AUC), in which the true positive rate (sensitivity) is plotted against the false positive rate (1-specificity) and each point represents a sensitivity/specificity corresponding to a decision threshold. The area under the curve (AUC) measures the classifier's discriminative ability, where a perfect classifier would have an AUC of 1 corresponding to 100% sensitivity and specificity.

eTable 1. qRT-PCR Primers for 79 Immune and Barrier Mediators

Gene Symbol	Assay ID
CCL2	Hs00234140_m1
CCL3	Hs00234142_m1
CCL4	Hs99999148_m1
CCL11*	HS00237013_m1
CCL17	Hs00171074_m1
CCL18	Hs00268113_m1
CCL20	Hs00355476_m1
CCL22	Hs01574247_m1
CCL26	Hs00171146_m1
CCR4	Hs99999919_m1
CD3	Hs00174158_m1
CD11b	Hs00167304_m1
CD11c	Hs00174217_m1
CD25	Hs00907779_m1
CD28	Hs01007422_m1
CD83	Hs00188486_m1
CD123	Hs00608141_m1
CD209	Hs01588349_m1
CDSN	Hs00169911_m1
CERS3	Hs00698859_m1
CLDN1	Hs00221623_m1
CLDN8	Hs04186769_s1
CLDN23	Hs01013638_s1
CSF1	Hs00174164_m1
CSF2	Hs00929873_m1
CXCL1	Hs00236937_m1
CXCL9	Hs00171065_m1
CXCL10	Hs01124252_g1
CXCL11	Hs00171138_m1
DEFB4B	Hs00823638_m1
DGAT2	Hs01045913_m1
ELOVL3*	Hs00537016_m1
ELVOL5	Hs01094711_m1
FA2H	Hs00757813_m1
FAR2	Hs00216461_m1
FcεRI	Hs00175408_m1
FLG	Hs00856927_g1
FLG2	Hs00418578_m1
FOXP3	Hs01085834_m1
IFN _γ	Hs00989291_m1
IL1 _α	Hs00174092_m1
IL1 _β	Hs00174097_m1
IL-1RA	Hs00893626_m1
IL-2	Hs00174114_m1
IL-4	Hs00174122_m1
IL4R	Hs00965056_m1
IL-6	Hs00985639_m1
IL-8	Hs00174103_m1
IL-10	Hs00961622_m1
IL-12/IL-23p40	Hs01011518_m1
IL-13	Hs00174379_m1
IL17C	Hs00171163_m1
IL-19	Hs00604657_m1
IL-23p19	Hs00900828_g1
IL-33	Hs04931857_m1

IL-34	Hs01050926_m1
IL-36G	Hs00219742_m1
IL-37	Hs00367201_m1
ICOS	Hs00359999_m1
K16	Hs00955082_g1
KLK5	Hs01548153_m1
KLK7	Hs00192503_m1
Langerin	Hs00210453_m1
LL37	Hs00189038_m1
LOR	Hs01894962_s1
MMP12	Hs00159178_m1
MX1	Hs00895608_m1
OX40L	Hs04400731_m1
PI3	Hs00160066_m1
PPL	Hs00160312_m1
PSORS1C2	Hs00204152_m1
S100A7	Hs01923188_u1
S100A8	Hs00374264_g1
S100A9	Hs00610058_m1
S100A12	Hs00942835_g1
SCD	Hs01682761_m1
SERPINB3	Hs00199468_m1
STAT1	Hs01013996_m1
STAT3	Hs00374280_m1

qRT-PCR, quantitative real-time polymerase chain reaction; *Markers that were evaluated, but not detected in tape-strips.

eTable 2. Immunohistochemistry Antibodies

Antigen	Manufacturer	Clone	Isotype	Dilution
CD11b	BD Pharmingen	Mouse	IgG1	1:50
IL-33	ThermoFisher	Mouse	IgG1	1:2,000
IL-17C	LSBio	Rabbit	IgG	1:100

eTable 3. Summary of Past Tape-Strip Studies in Patients With Atopic Dermatitis

Reference	Markers/content evaluated	No. of mediators detected/evaluated	Analysis method	Type: No. of tape-strips used for analysis/total collected	No. of subjects	Age group (years)	Tissue evaluated
Evaluation of immune mediators and receptors							
Leung et al., 2019	CCR8, IL-4R, CRLF2, CCL17, CCL22, IL-13, IL-7R, etc.	96/218 ^a	RNA Ampliseq Transcriptome sequencing	D-Squame: 11-20/30	AD LS: 40 AD NL: 40 HC: 22	8-16	LS, NL, N
Berdyshev et al., 2018	ELOVL 1-7, IL-13, IL-4R	NA	RNA Ampliseq Transcriptome sequencing	D-Squame: 11-20/20	AD LS: 15 AD NL: 30 HC: 25	≥18	LS, NL, N
Dyjack et al., 2018	CYSLTR1, SPRR2F, MMP9, MMP10, etc.	29 ^b	RNA AmpliSeq whole-transcriptome sequencing	D-Squame: 11-20/20	AD: 30 HC: 25	≥18	LS, NL, N
Hulshof et al., 2018	IL-1 α , IL-1 β , IL-18, IL-13, IL-14, CCL2, CCL4, CXCL8, CXCL10, CCL11, CCL13, CCL17, CCL22, etc.	13/28	MESO QuickPlex SQ 120 Assay	D-Squame: 5 th or 6 th /6	AD: 53 HC: 50	<12	LS, NL, N
McAleer et al., 2018	IL-1 α , IL-1 β , IL-2, IL-5, IL-7, IL-8, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-18, CSF2, CCL2, CCL3, CCL4, CCL13, CCL17, CCL22, CXCL10, etc.	19/27	MESO QuickPlex SQ 120 Assay	D-Squame: 5 th /8	AD: 66 HC: 13	<1	NL, N
Tham et al., 2018	OR10G7, ORs, etc.	381	RNA Ampliseq transcriptome sequencing	D-Squame: 11-20/20	AD: 30 HC: 25	≥18	LS, NL, N
Koppes et al., 2016	CSF2, IFN γ , IL-1 α , IL-1 β , IL-2, IL-4, IL-5, IL-8, IL-10, IL-12/IL-23p40, IL-13, IL-16, IL-17a, CCL2, CCL3, CCL4, CCL11,	24/38	MESO QuickPlex SQ 120 assay	D-Squame: 6 th /8	AD: 90 HC: 20	≥18	LS, NL, N

	CCL13, CCL22, CCL17, etc.						
Amarbayasgalan et al., 2013	IL-8, IL-18, VEGF, TGF- α	4	ELISA	Cellotape: 1/1	AD: 50 HC: 12	≥ 18	LS, NL, N
Morita et al., 2010	CCL17	1	TARC-specific antibody	Cellotape: 1/1	AD: 61 HC: 19	≥ 17	LS, N
Evaluation of proteins/stratum corneum integrity/lipid composition							
Berdyshev et al., 2018	Short-chain ceramides, SMs, LPCs	NA	HPLC-ESI-MS;	D-Squame: 5 th and 6 th /20	AD LS: 15 AD NL: 30 HC: 25	≥ 18	LS, NL, N
Clausen et al., 2018	hBD-2, hBD-3, RNase 7, psoriasin, LL37	4/5	ELISA	D-Squame: pooled in groups of 5/35	AD: 9 HC: 5	≥ 18	LS, NL, N
Dapic et al., 2018	FFAs	NA	LC-ESI-MS	D-Squame: 4-9/9	AD: 6 HC: 4	≥ 1	LS, N
Reference	Markers/content evaluated	No. of mediators detected/evaluated	Analysis method	Type: No. of tape-strips used for analysis/total collected	No. of subjects	Age group (years)	Tissue evaluated
Reisdorph et al., 2018	α -enolase, FLG2, FLG1, SERPINB3, etc.	14peptides/7proteins	Tandem mass spectrometry	D-Squame: 10/20	AD: 6 HC: 6	≥ 18	LS, N
Clausen et al., 2016	Cumulative soluble and total protein	NA	Squame Scan, Micro BCA protein determination kit	D-Squame: pooled in groups of 5/35	AD: 9 HC: 5	≥ 18	LS, NL, N
Leitch et al., 2016	TEWL	NA	Tewameter TM300	D-Squame: ~10-40	AD: 58 HC: 26	≥ 18	LS, N
Winget et al., 2016	SERPINA3, SERPINB3, SERPINB5, Keratins, FLG-2, etc.	252/1102 ^c	Mass spectrometry	D-Squame: 8/8	AD: 11 HC: 17	≥ 18	LS, NL, N
Riethmuller et al., 2015	NMFs, corneocytes	NA	HPLC; AFM	D-Squame: 5 th ; 7 th /8	AD: 15	<3	LS
Clausen et al., 2013	hBD-2, total protein	1	ELISA, Micro BCA Protein Assay	D-Squame: 2-16/16	AD: 25 HC: 11	≥ 18	LS, NL, N
Janssens et al., 2012	Ceramide composition and lipid organization	NA	Mass spectrometry, infrared spectroscopy, X-ray diffraction	D-Squame: 6-9/9	AD: 15 HC: 28	≥ 18	NL, N
Angelova-Fischer et al., 2011	SC integrity/cohesion, epidermal barrier recovery, lipid analysis	NA	Tewameter TM300, Squame Scan; Large Finn Chamber; AMD-HPTLC	D-Squame: 2, 10, 20, 30 /30	AD: 37/25 HC: 20/18 ^d	≥ 18	LS, NL, N

Kezic et al., 2011	NMFs	NA	HPLC	D-Squame: 2-5 /5	AD: 96 HC: 24	<18	NL, N
Broccardo et al., 2009	α -enolase, SERPINB3, dermcidin, etc.	53	HPLC	D-Squame: pooled in groups of 5/20	AD: 5 HC: 5	\geq 18	LS, NL, N
Voegeli et al., 2009	SC tryptase-like enzyme, KLK5, KLK7, etc; Total protein, SC integrity	6	Squame Scan, RP-HPLC	D-Squame: pooled in groups of 5 /20	AD: 12 HC: 6	\geq 18	LS, NL, N

LPC, lysophosphatidylcholines; *SMs*, sphingomyelins; *ELOVL 1-7*, elongases 1-7 ; *HPLC-ESI-MS*, High Performance Liquid chromatography-electrospray ionization-tandem mass spectrometry; *FFAs*, free fatty acids; *hBD-2*, human beta defensin-2; *hBD-3*, human beta defensin-3; *CSF*, colony-stimulating factor; *FLG*, filaggrin; *ORs*, olfactory receptors ; *VEGF*, vascular endothelial growth factor; *TGF- α* , transforming growth factor-alpha; *NMFs*, natural moisturizing factors; *SC*, stratum corneum; *HPLC*, High-performance liquid chromatography; *AMD-HPTLC*, Automated development high-performance thin layer chromatography; *AFM*, Atomic force microscopy; *RP-HPLC*, reverse-phase high-performance liquid chromatography; *TARC*, thymus and activation-regulated chemokine; *AD*, atopic dermatitis; *HC*, healthy controls; *LS*, lesional; *NL*, non-lesional; *N*, normal; *NA*, not applicable; ^aDifferentially expressed genes within nonlesional tape strips of patients with AD and food allergies/FA+, those without AD FA-, and non-atopics; yielded a set of 288 genes that separated patients from controls (n=51), those with AD FA- (n=19), and those with AD FA+ (n=218); AD FA+ enriched genes overlapped with gene signature previously identified in patients with type 2 high AD (n=96/218); ^b29 differentially expressed genes were identified between nonlesional AD and healthy controls, 656 differentiated genes were expressed in analysis of nonlesional skin RNA transcripts of AD patients exhibiting a type 2 high AD endotype (n=9) and patients with AD not exhibiting the type 2 immune-activation signature (n=9), i.e CCR4, CCL22, CD80, CD86, CD28, CD3, etc.; ^c252 proteins were differentially observed between healthy and AD samples, combining all spectral evidence 1,102 proteins were identified at a 1% false positive error rate;^d37AD patients (14 patients with filaggrin-AD and 23 patients with non-filaggrin AD) and 20 healthy controls participated in assessment of epidermal barrier function and stratum corneum integrity/cohesion, 25 AD patients and 18 healthy controls volunteered for monitoring of the epidermal barrier recovery.

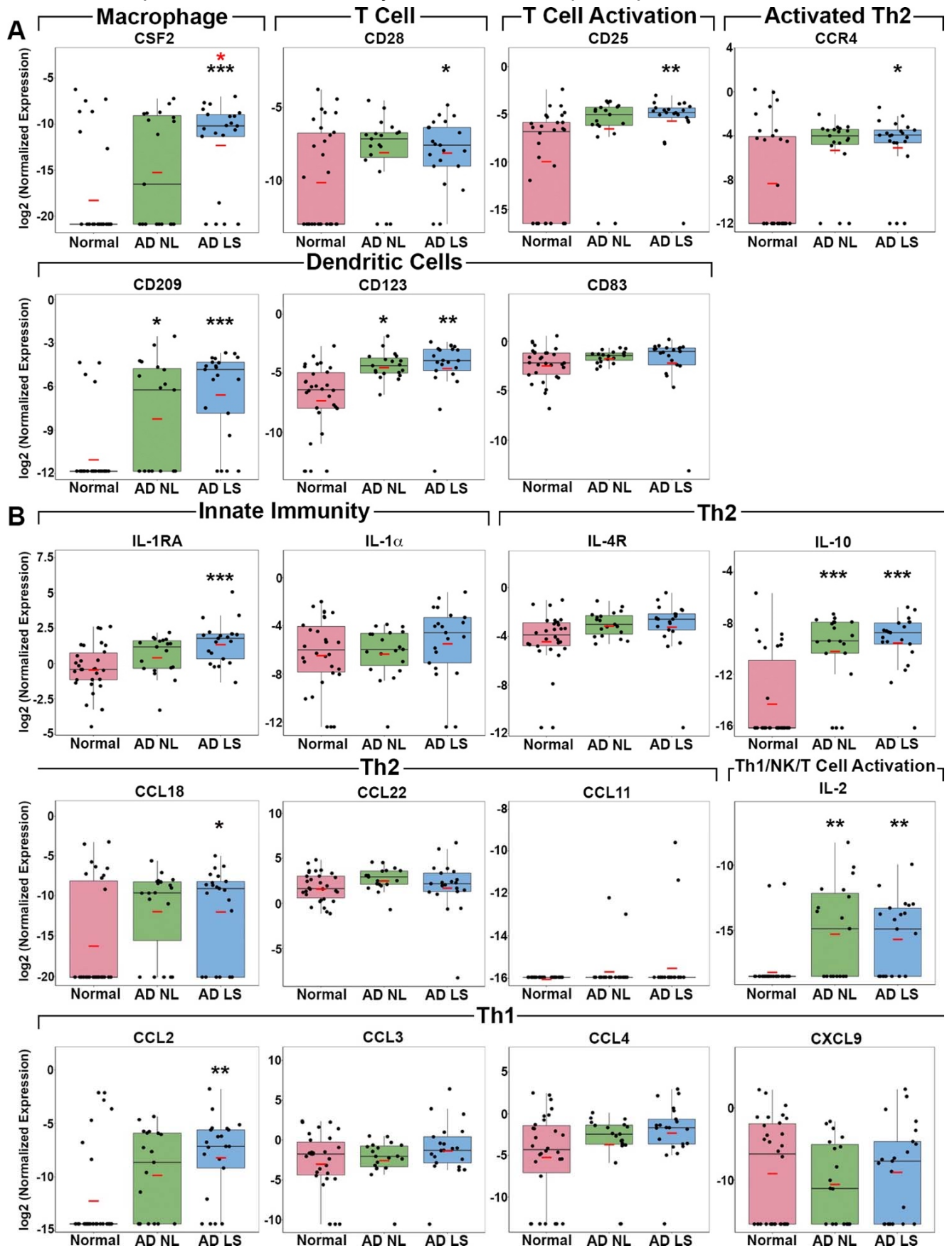
eTable 4. Means, Standard Errors, and Confidence Intervals for All Immune and Barrier Biomarkers

	Normal mean	Normal SE	Normal CI Lower	Normal CI Upper	NL AD mean	NL AD SE	NL AD CI Lower	NL AD CI Upper	LS AD mean	LS AD SE	LS AD CI Lower	LS AD CI Upper
MMP12	-1.779	0.707	-2.486	-1.071	2.003	0.303	1.701	2.306	2.226	0.343	1.883	2.568
PI3	-0.438	0.426	-0.864	-0.012	0.135	0.482	-0.346	0.617	0.455	0.711	-0.256	1.166
PPL	-0.238	0.298	-0.536	0.061	-2.710	0.392	-3.102	-2.318	-3.299	0.697	-3.996	-2.602
CD11b	-7.824	0.968	-8.792	-6.856	-4.636	0.884	-5.520	-3.751	-2.599	0.738	-3.336	-1.861
CDSN	3.648	0.341	3.307	3.988	1.996	0.520	1.476	2.516	1.970	0.807	1.163	2.777
CXCL10	-13.970	1.046	-15.015	-12.924	-	0.664	-	-	-	1.004	-	-
					15.234		15.898	14.570	13.052		14.056	12.048
CXCL9	-8.843	1.320	-10.163	-7.522	-	1.313	-	-9.038	-8.656	1.419	-	-7.237
					10.351		11.664				10.075	
CCL17	-2.676	0.788	-3.464	-1.887	1.762	0.303	1.459	2.065	1.544	0.712	0.833	2.256
CXCL11	-11.265	0.835	-12.100	-10.430	-	0.652	-	-	-	0.846	-	-
					12.512		13.163	11.860	11.585		12.430	10.739
CCL26	-19.113	0.000	-19.113	-19.113	-	1.115	-	-	-	1.206	-	-
					15.153		16.268	14.038	13.466		14.672	12.260
CSF1	-4.542	0.675	-5.217	-3.867	-2.502	0.559	-3.060	-1.943	-1.322	0.515	-1.837	-0.806
CD11c	-4.004	0.782	-4.786	-3.222	-1.906	0.270	-2.175	-1.636	-1.701	0.650	-2.352	-1.051
FcεRI	-2.494	0.697	-3.191	-1.797	-0.277	0.268	-0.545	-0.008	0.081	0.619	-0.538	0.700
LL37	-15.628	0.928	-16.555	-14.700	-	1.444	-	-	-9.927	1.410	-	-8.517
					11.809		13.252	10.365			11.336	
SERPINB3	-0.649	0.473	-1.123	-0.176	2.718	0.433	2.286	3.151	3.090	0.548	2.542	3.639
PSORS1C2	-3.707	0.622	-4.330	-3.085	-6.781	1.089	-7.870	-5.692	-6.507	0.924	-7.431	-5.584
CD207	-12.087	0.789	-12.876	-11.297	-6.260	0.901	-7.161	-5.359	-5.886	0.883	-6.769	-5.004
CLDN1	-2.925	0.737	-3.661	-2.188	-0.423	0.292	-0.715	-0.130	-0.587	0.383	-0.970	-0.204
CCL2	-12.044	0.811	-12.855	-11.232	-9.657	0.929	-	-8.727	-8.013	0.818	-8.831	-7.194
							10.586					
CCL3	-2.764	0.696	-3.460	-2.068	-2.316	0.560	-2.876	-1.756	-1.108	0.743	-1.851	-0.364
CXCL1	-4.663	0.798	-5.461	-3.866	-3.049	1.122	-4.171	-1.927	-0.902	0.824	-1.726	-0.078
CCL11	-15.954	0.000	-15.954	-15.954	-	0.245	-	-	-	0.364	-	-
					15.600		15.845	15.356	15.434		15.797	15.070
CCL18	-15.982	1.185	-17.167	-14.797	-	1.214	-	-	-	1.224	-	-
					11.699		12.913	10.485	11.736		12.960	10.511
CCL20	-10.757	0.781	-11.539	-9.976	-6.579	0.707	-7.285	-5.872	-6.013	0.580	-6.593	-5.433
S100A8	-0.712	0.357	-1.069	-0.355	1.168	0.380	0.789	1.548	1.233	0.628	0.604	1.861
STAT3	-4.071	0.366	-4.437	-3.706	-3.347	0.298	-3.645	-3.049	-2.653	0.657	-3.310	-1.996
FLG2	1.651	0.402	1.249	2.053	-1.466	0.670	-2.136	-0.796	-3.100	0.698	-3.799	-2.402
ELOVL3	-17.423	0.810	-18.233	-16.612	-	0.249	-	-	-	0.725	-	-
					19.002		19.251	18.753	18.045		18.770	17.320
S100A9	1.191	0.362	0.830	1.553	2.918	0.302	2.616	3.220	3.291	0.519	2.772	3.810
FA2H	-5.414	1.108	-6.522	-4.307	-	1.398	-	-	-	1.112	-	-
					12.869		14.267	11.471	15.917		17.029	14.804
DEFB4B	-2.831	0.722	-3.553	-2.110	0.586	0.410	0.176	0.996	0.349	0.826	-0.477	1.175
FLG	2.182	0.453	1.729	2.635	-1.702	0.566	-2.267	-1.136	-2.885	0.421	-3.306	-2.463
MX1	-3.778	0.707	-4.485	-3.070	-3.657	0.836	-4.493	-2.822	-1.805	0.768	-2.573	-1.037
S100A12	-10.155	0.861	-11.016	-9.294	-6.811	0.749	-7.560	-6.062	-5.928	0.599	-6.528	-5.329
STAT1	-4.079	0.675	-4.755	-3.404	-2.819	0.393	-3.212	-2.426	-1.888	0.638	-2.525	-1.250
DGAT2	-2.537	0.571	-3.109	-1.966	-2.541	0.415	-2.955	-2.126	-1.724	0.612	-2.336	-1.113
ELOVL5	-7.405	0.864	-8.269	-6.541	-5.542	0.538	-6.080	-5.005	-4.929	0.606	-5.535	-4.323
CCL22	1.790	0.291	1.498	2.081	2.689	0.283	2.406	2.972	1.904	0.637	1.267	2.542
CD209	-10.901	0.440	-11.340	-10.461	-8.083	0.860	-8.943	-7.223	-6.433	0.663	-7.096	-5.770
LOR	5.941	0.437	5.505	6.378	2.289	0.660	1.629	2.950	1.272	0.526	0.746	1.799
S100A7	-1.523	0.354	-1.878	-1.169	0.441	0.485	-0.044	0.925	0.264	0.586	-0.322	0.850
CLDN8	-15.847	1.171	-17.018	-14.676	-	0.810	-	-	-	1.055	-	-
					18.336		19.146	17.526	17.825		18.880	16.770

OX40L	-16.646	0.513	-17.159	-16.133	-	0.900	-	-	-	0.838	-	-
					12.740		13.640	11.840	13.228		14.066	12.390
CCL4	-5.014	0.950	-5.964	-4.065	-3.458	0.856	-4.314	-2.602	-2.100	0.747	-2.846	-1.353
CCR4	-8.143	0.857	-9.000	-7.285	-5.134	0.720	-5.854	-4.414	-4.900	0.676	-5.577	-4.224
CD28	-9.996	0.632	-10.628	-9.364	-7.950	0.575	-8.525	-7.376	-7.968	0.494	-8.462	-7.474
CD3	-14.170	0.995	-15.165	-13.175	-9.397	0.950	-	-8.447	-8.879	0.719	-9.598	-8.160
							10.347					
CD83	-2.289	0.307	-2.597	-1.982	-1.566	0.138	-1.704	-1.428	-2.007	0.613	-2.620	-1.393
CERS3	-5.885	0.438	-6.323	-5.447	-5.483	0.441	-5.924	-5.042	-6.338	0.562	-6.900	-5.776
CLDN23	-8.870	0.682	-9.553	-8.188	-	0.698	-	-	-	0.624	-	-
					10.902		11.600	10.204	11.322		11.947	10.698
CSF2	-18.079	0.965	-19.044	-17.114	-	1.376	-	-	-	1.076	-	-
					15.037		16.413	13.661	12.099		13.175	11.023
FAR2	-6.654	0.590	-7.243	-6.064	-7.647	0.563	-8.210	-7.083	-7.569	0.516	-8.085	-7.054
FOXP3	-9.692	0.755	-10.446	-8.937	-7.098	0.870	-7.969	-6.228	-5.905	0.477	-6.381	-5.428
ICOS	-16.769	1.001	-17.770	-15.768	-	1.007	-	-	-	0.807	-	-
					11.387		12.393	10.380	11.286		12.093	10.479
IFNγ	-18.757	0.730	-19.487	-18.026	-	0.974	-	-	-	0.890	-	-
					17.161		18.136	16.187	17.082		17.972	16.192
IL-1RA	-0.306	0.305	-0.611	-0.000	0.566	0.321	0.245	0.887	1.488	0.318	1.170	1.806
IL-3RA	-7.157	0.558	-7.714	-6.599	-4.365	0.256	-4.621	-4.109	-4.436	0.531	-4.967	-3.905
IL-10	-14.176	0.610	-14.785	-13.566	-	0.683	-	-9.366	-9.386	0.470	-9.856	-8.916
					10.049		10.733					
IL-13	-14.209	0.766	-14.974	-13.443	-	1.143	-	-	-9.071	0.708	-9.779	-8.363
					12.134		13.278	10.991				
IL-17C	-13.642	0.834	-14.476	-12.808	-	0.848	-	-	-	0.740	-	-
					12.444		13.292	11.597	11.734		12.475	10.994
IL-19	-16.178	1.072	-17.250	-15.105	-	1.507	-	-	-9.015	1.106	-	-7.909
					12.233		13.740	10.726			10.122	
IL-1α	-6.301	0.546	-6.847	-5.756	-6.188	0.483	-6.671	-5.706	-5.331	0.669	-6.000	-4.663
IL-1β	-4.859	0.376	-5.235	-4.482	-3.943	0.388	-4.331	-3.555	-2.969	0.464	-3.433	-2.505
IL-2	-18.041	0.324	-18.366	-17.717	-	0.821	-	-	-	0.622	-	-
					15.132		15.953	14.310	15.521		16.143	14.899
IL-2RA	-9.755	0.941	-10.696	-8.813	-6.312	0.861	-7.172	-5.451	-5.492	0.609	-6.101	-4.883
IL-33	-13.111	0.979	-14.090	-12.133	-	0.853	-	-	-	0.869	-	-
					15.278		16.130	14.425	12.506		13.375	11.637
IL-34	-6.610	0.607	-7.217	-6.002	-	0.963	-	-9.320	-	1.045	-	-
					10.283		11.246		13.092		14.137	12.047
IL-36G	-3.345	0.374	-3.719	-2.971	-1.208	0.414	-1.622	-0.794	-1.404	0.549	-1.953	-0.855
IL-37	-1.722	0.355	-2.077	-1.367	-4.604	0.647	-5.251	-3.957	-5.877	0.829	-6.707	-5.048
IL-4	-19.460	0.481	-19.941	-18.979	-	0.883	-	-	-	0.906	-	-
					16.844		17.727	15.961	15.196		16.101	14.290
IL-4R	-4.287	0.439	-4.726	-3.849	-2.996	0.230	-3.227	-2.766	-3.076	0.482	-3.558	-2.594
IL-6	-18.132	0.814	-18.947	-17.318	-	1.292	-	-	-	0.776	-	-9.485
					13.950		15.243	12.658	10.262		11.038	
IL-8	-0.283	0.333	-0.615	0.050	1.404	0.433	0.971	1.838	2.373	0.490	1.883	2.863
K16	-1.170	0.309	-1.479	-0.861	-0.804	0.396	-1.200	-0.407	-0.582	0.473	-1.055	-0.110
KLK5	1.044	0.287	0.757	1.331	-1.383	0.491	-1.874	-0.891	-1.950	0.360	-2.310	-1.591
KLK7	-1.362	0.305	-1.667	-1.058	-2.538	0.399	-2.937	-2.138	-2.848	0.528	-3.376	-2.320
SCD	-4.792	0.546	-5.338	-4.246	-6.120	0.573	-6.693	-5.546	-6.296	0.452	-6.748	-5.844
IL-12/IL-23p40	-15.413	0.843	-16.256	-14.570	-	1.199	-	-	-	0.886	-	-
					12.914		14.113	11.715	11.097		11.983	10.212
IL-23p19	-14.762	1.140	-15.902	-13.622	-9.042	1.193	-	-7.849	-7.671	0.710	-8.381	-6.960
							10.234					

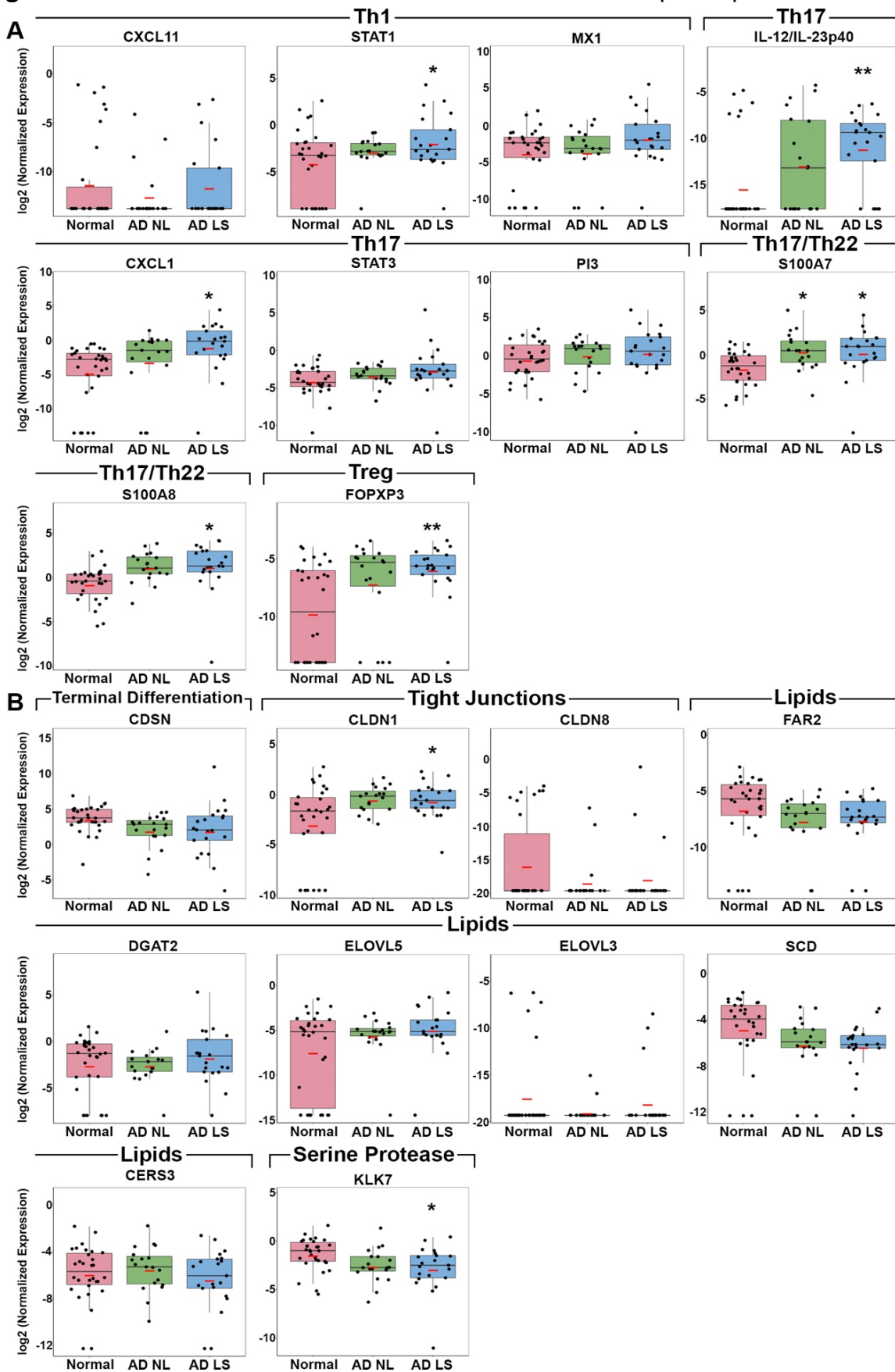
SE, standard error; CI, confidence interval; NL, nonlesional; LS, lesional; AD, atopic dermatitis.

eFigure 1. Gene Expression of Inflammatory Biomarkers in Tape Strips



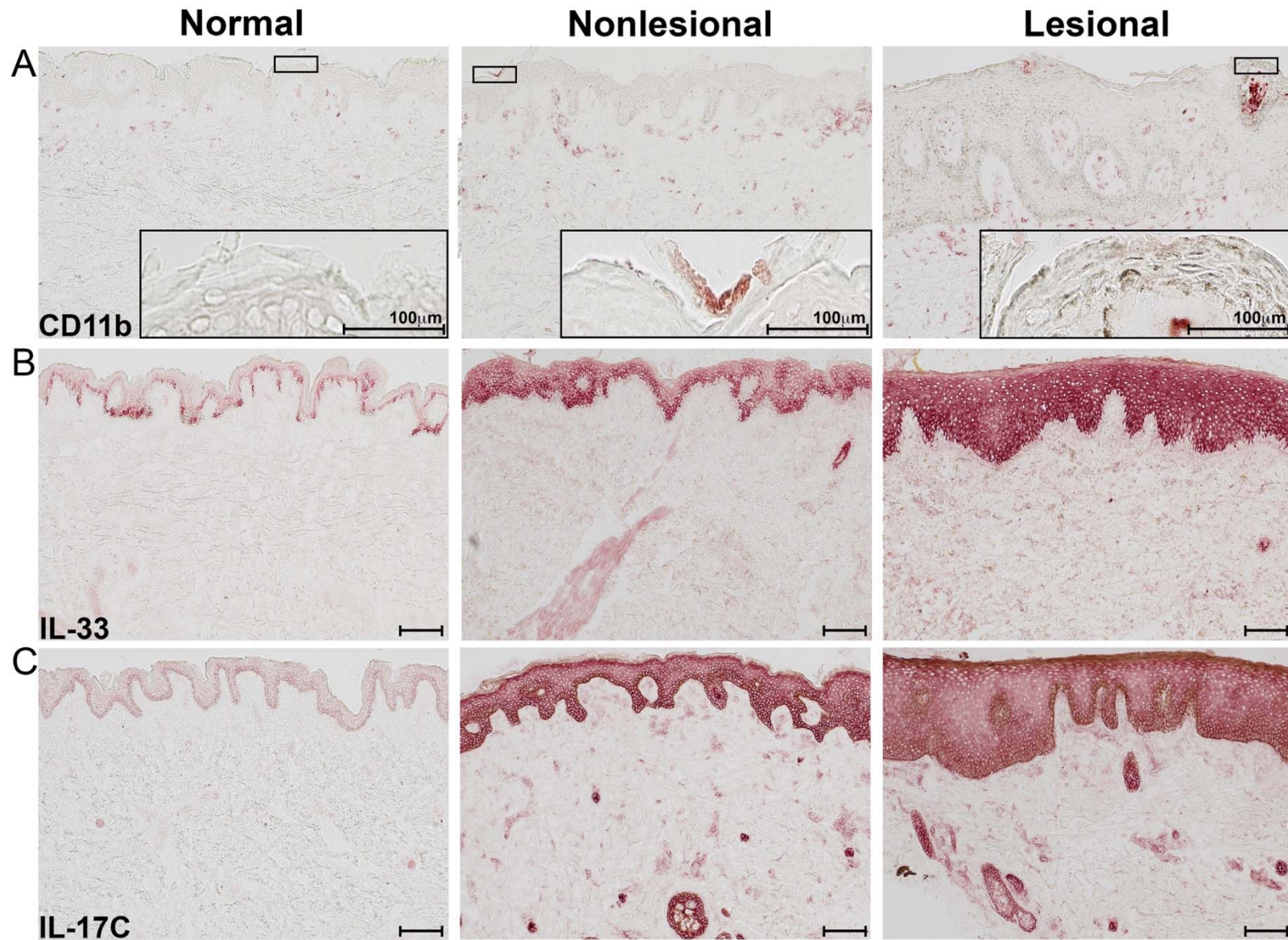
Additional cellular markers detected in tape-strips in normal, AD nonlesional (NL), and AD lesional skin (LS) (A). Multiple immune axes biomarkers detected in tape-strips (B). * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. *Black stars*: significance of comparison between AD skin and normal skin; *red stars*: significance of comparison between AD lesional skin versus nonlesional skin.

eFigure 2. Immune and Barrier AD Biomarkers Detected in Tape Strips



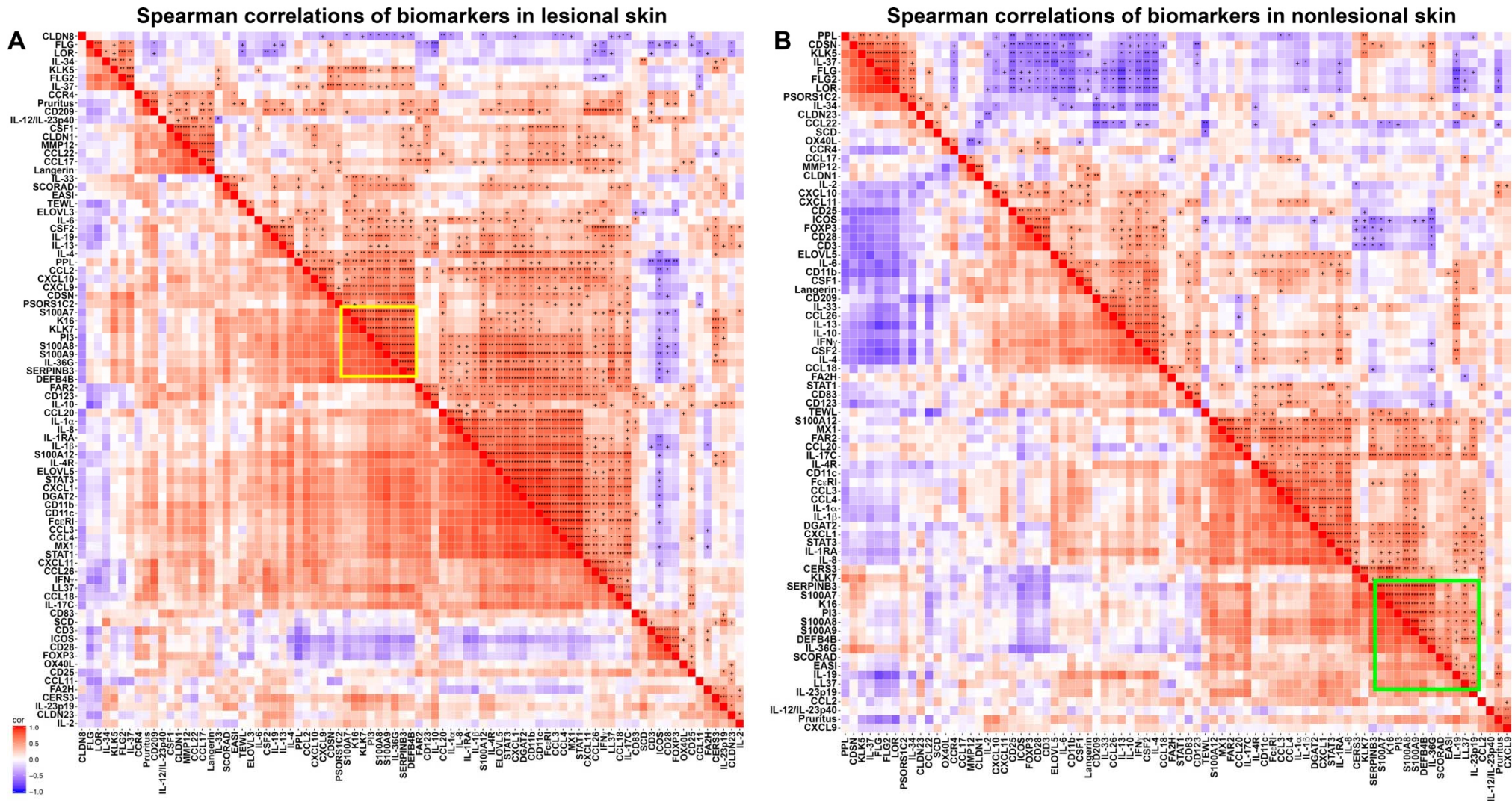
Additional immune biomarkers show differences in normal, AD nonlesional (NL), and AD lesional skin (LS) using tape-strips (A). Additional barrier biomarkers detected in tape-strips across AD tissues versus normal skin (B). * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. Black stars: significance of comparison between AD skin and normal skin.

eFigure 3. Histology



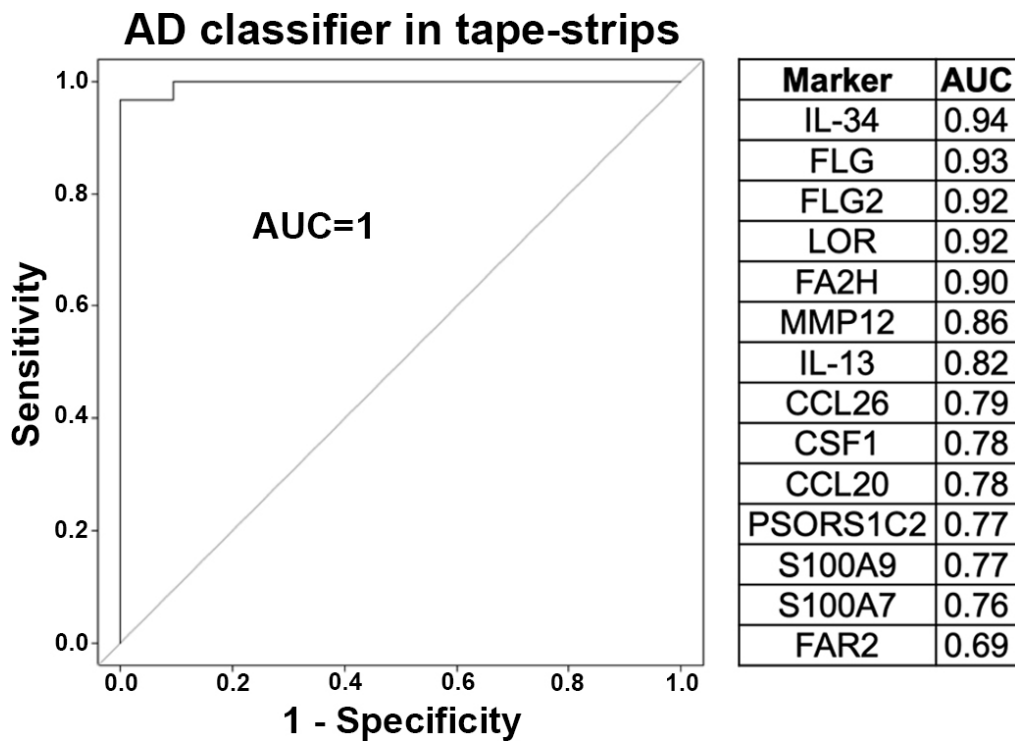
Representative immunohistochemistry staining, 10x magnification, in pediatric patients with AD and control subjects of CD11b (A), IL-33 (B), and IL-17C (C). 40x magnification inserts illustrates absence or presence of CD11b+ cellular infiltrates in outer epithelial layers in normal, nonlesional, and lesional AD skin (A).

eFigure 4. Expression of Biomarkers in Tape Strips Correlates With Clinical Severity



Heatmap of Spearman correlation matrix of measured values in pediatric AD lesional skin using tape-strips (A). *Yellow box* denotes Th17/Th22 cluster. Heatmap of Spearman correlation matrix of measured values in pediatric AD nonlesional skin using tape-strips (B). *Green box* denotes Th17/Th22 cluster. Horizontal rows for each marker show shades of blue-violet for negative correlations and white-red for positive correlations. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

eFigure 5. Receiver Operating Characteristic Area Under the Curve (ROC AUC) in Tape Strips



An integrated classifier of immune markers and skin barrier genes accurately discriminates AD and normal patients (AUC=1). The AUC values of single gene classifiers are provided in a table.

eReferences

1. Kelleher MM, Dunn-Galvin A, Gray C, Murray DM, Kiely M, Kenny L, et al. Skin barrier impairment at birth predicts food allergy at 2 years of age. *J Allergy Clin Immunol*. 2016;137(4):1111-6.e8. doi:10.1016/j.jaci.2015.12.1312.