Use of Tape Strips to Detect Immune and Barrier Abnormalities in the Skin of Children With Early-Onset Atopic Dermatitis

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Background

- Skin biopsies
  - Gold standard for biomarker analysis in atopic dermatitis (AD)
  - Often not feasible for children
- Tape strips
  - Minimally invasive and non-scarring approach
  - Feasible for pediatric longitudinal drug studies or clinical trials

Methods

- 16 tape strips from nonlesional (forearm) and lesional (antecubital) skin of 21 AD children
  - Under 5yo, <6mo from onset, moderate to severe disease
  - Exclusions: Patients with active skin infections, systemic immunosuppressants within 4 weeks, topical steroids or immunomodulators within 1 week or moisturizer at tape-strip site
- 16 tape strips collected from nonlesional (forearm) skin of 30 healthy children
- Gene expression evaluated using qRT-PCR

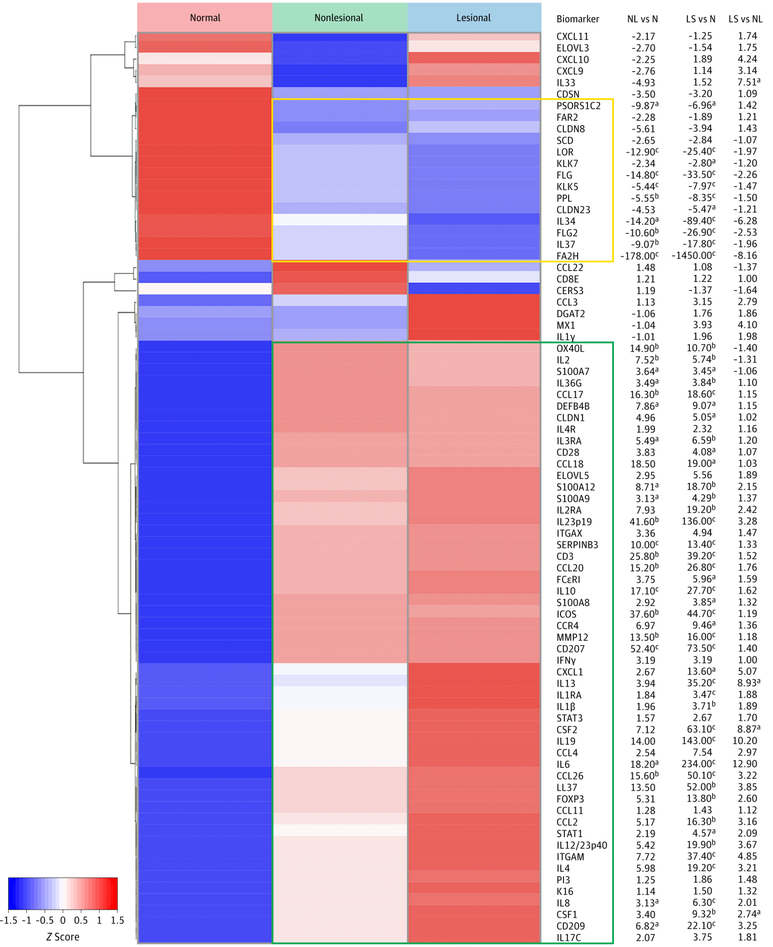
Baseline Demographics and Clinical Characteristics

Characteristic	Children With AD (n = 21)[a]	Children Without AD (n = 30)	*P* Value
Age, mean (SD), y	1.7 (1.7)	1.8 (2.0)	.85
Sex, No. (%)			
Female	6 (28.6)	20 (66.7)	.02
Male	15 (71.4)	10 (33.3)	
Race/ethnicity, No. (%)			
Asian/Pacific Islander	2 (9.5)	6 (20.0)	.30
African American	4 (19.0)	2 (6.7)	
White	15 (71.4)	22 (73.3)	
Clinical severity disease scores, mean (SD)			
SCORAD	54.4 (21.2)	NA	NA
EASI	20.9 (12.6)	NA	NA
TEWL, lesional, g/h/m^2	65.4 (49.2)	NA	NA
TEWL, nonlesional, g/h/m^2	28.1 (18.1)	NA	NA
Pruritus ADQ	16.6 (8.1)	NA	NA
Patient history			
Age at onset of AD, mean (SD), mo	2.3 (1.3)	NA	NA
History of atopy, No. (%)	6 (28.6)	NA	NA
Family history of AD, No. (%)	18 (87.7)	NA	NA

Abbreviations: AD, atopic dermatitis; ADQ, Atopic Dermatitis Quickscore; EASI, Eczema Area and Severity Index; NA, not applicable; SCORAD, SCORing Atopic Dermatitis; TEWL, transepidermal water loss.

[a] Normal value. Mean (SD) TEWL at age 2 months in children without AD has been reported as 10.97 (7.98) g/h/m^2 and at age 6 months has been reported as 10.71 (7.1) g/h/m^2.

Heat Map of Immune and Barrier Atopic Dermatitis (AD) Biomarkers Detected in Tape Strips

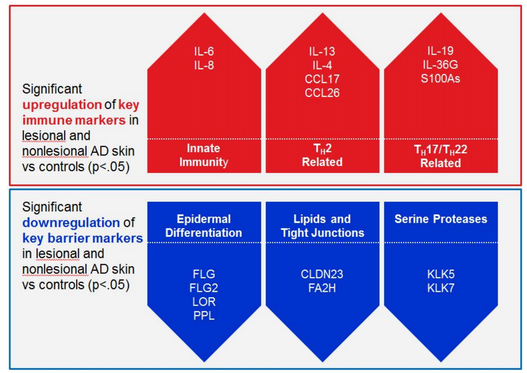


Biomarker	NL vs N	LS vs N	LS vs NL
CXCL11	-2.17	-1.25	1.74
ELOVL3	-2.70	-1.54	1.75
CXCL10	-2.25	1.89	4.24
CXCL9	-2.76	1.14	3.14
IL33	-4.93	1.52	7.51[a]
CDSN	-3.50	-3.20	1.09
PSORS1C2	-9.87[a]	-6.96[a]	1.42
FAR2	-2.28	-1.89	1.21
CLDN8	-5.61	-3.94	1.43
SCD	-2.65	-2.84	-1.07
LOR	-12.90[c]	-25.40[c]	-1.97
KLK7	-2.34	-2.80[a]	-1.20
FLG	-14.80[c]	-33.50[c]	-2.26
KLK5	-5.44[a]	-7.97[c]	-1.47
PPL	-5.55[b]	-8.35[c]	-1.50
CLDN23	-4.53	-5.47[a]	-1.21
IL34	-14.20[a]	-89.40[c]	-6.28
FLG2	-10.60[b]	-26.90[c]	-2.53
IL37	-9.07[b]	-17.80[c]	-1.96
FA2H	-178.00[c]	-1450.00[c]	-8.16
CCL22	1.48	1.08	-1.37
CD8E	1.21	1.22	1.00
CERS3	1.19	-1.37	-1.64
CCL3	1.13	3.15	2.79
DGAT2	-1.06	1.76	1.86
MX1	-1.04	3.93	4.10
IL1y	-1.01	1.96	1.98
OX40L	14.90[b]	10.70[b]	-1.40
IL2	7.52[b]	5.74[b]	-1.31
S100A7	3.64[a]	3.45[a]	-1.06
IL36G	3.49[a]	3.84[b]	1.10
CCL17	16.30[b]	18.60[c]	1.15
DEFB4B	7.86[a]	9.07[a]	1.15
CLDN1	4.96	5.05[a]	1.02
IL4R	1.99	2.32	1.16
IL3RA	5.49[a]	6.59[b]	1.20
CD28	3.83	4.08[a]	1.07
CCL18	18.50	19.00[a]	1.03
ELOVL5	2.95	5.56	1.89
S100A12	8.71[a]	18.70[b]	2.15
S100A9	3.13[a]	4.29[b]	1.37
IL2RA	7.93	19.20[b]	2.42
IL23p19	41.60[b]	136.00[c]	3.28
ITGAX	3.36	4.94	1.47
SERPINB3	10.00[c]	13.40[c]	1.33
CD3	25.80[b]	39.20[c]	1.52
CCL20	15.20[b]	26.80[c]	1.76
FCεRI	3.75	5.96[c]	1.59
IL10	17.10[c]	27.70[c]	1.62
S100A8	2.92	3.85[a]	1.32
ICOS	37.60[b]	44.70[c]	1.19
CCR4	6.97	9.46[a]	1.36
MMP12	13.50[b]	16.00[c]	1.18
CD207	52.40[c]	73.50[c]	1.40
IFNγ	3.19	3.19	1.00
CXCL1	2.67	13.60[a]	5.07
IL13	3.94	35.20[c]	8.93[a]
IL1RA	1.84	3.47[c]	1.88
IL1β	1.96	3.71[c]	1.89
STAT3	1.57	2.67	1.70
CSF2	7.12	63.10[c]	8.87[a]
IL19	14.00	143.00[c]	10.20
CCL4	2.54	7.54	2.97
IL6	18.20[a]	234.00[c]	12.90
CCL26	15.60[b]	50.10[c]	3.22
LL37	13.50	52.00[b]	3.85
FOXP3	5.31	13.80[b]	2.60
CCL11	1.28	1.43	1.12
CCL2	5.17	16.30[b]	3.16
STAT1	2.19	4.57[a]	2.09
IL12/23p40	5.42	19.90[b]	3.67
ITGAM	7.72	37.40[c]	4.85
IL4	5.98	19.20[c]	3.21
PI3	1.25	1.86	1.48
K16	1.14	1.50	1.32
IL8	3.13[a]	6.30[c]	2.01
CSF1	3.40	9.32[b]	2.74[a]
CD209	6.82[a]	22.10[c]	3.25
IL17C	2.07	3.75	1.81

Mean expression levels of all 79 barrier and inflammatory mediators detected using tape strips (measured by qRT-PCR). Biolarkers with significant fold-changes in non-lesional (NL) vs. normal (N) skin, lesional (LS) AD vs. normal age-matched skin, and LS AD vs. NL AD skin. [a]p<0.05; [b]p<0.01; [c]p<0.001.

Results

- 99% yielded sufficient mRNA (70 of 71 samples)
- 97% of immune and barrier genes detected (77 of 79 genes)
- 53 of 79 markers - significant difference between lesional/nonlesional AD vs. controls
- Significant downregulation of negative immune regulators (IL-34/IL-37, p<.05)
- Significant correlations between Th2 (IL-33/IL4R) and Th17/Th22 (IL-36G/S100As) products in lesional/nonlesional AD skin and disease severity (SCORAD/EASI/pruritus) or transepidermal water loss (TEWL)
- Nonlesional (NL) skin is **not** normal skin and NL skin abnormalities are influenced by lesional (L) skin activity
- AD-associated biomarkers (TH2, IL-33, IL-4R, CCR4, and CCL18) in nonlesional (NL) skin correlated highly with severity indices



Conclusions

Tape strips provide a minimally invasive approach to:

- Evaluate AD (and other disease) associated cutaneous biomarkers
- Potentially predict future course, comorbidities, and therapeutic responses

No previous tape strip study has been able to capture RNA data so comprehensively **(99% of specimens, 97% of key genes).**

Elevations in immune biomarkers and reductions in barrier genes are consistent with results in biopsy studies for young children with AD.

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