BIOMARKERS IN ATOPIC DERMATITIS (AD)

A review on behalf of the International Eczema Council

Biomarkers are potential instruments in the toolbox of precision medicine in AD.

Precision medicine approaches may improve AD management because therapeutic response may vary based on heterogeneous clinical and molecular phenotypes.

BIOMARKER DEFINITIONS

> A biological molecule found in blood, other body fluids, or tissues that can be used to follow body processes and diseases in humans and animals.
>
> EMA

> A defined characteristic that is measured as an indicator of normal biologic processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions.
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> FDA

DEMANDING PROCESS OF BIOMARKER DEVELOPMENT AND VALIDATION

STAGE 01 — BIOMARKER DISCOVERY
By chance or hypothesis-driven discovery using patient registries

STAGE 02 — INTERNAL VALIDATION
In a limited number of clinical cases

STAGE 03 — EXTERNAL VALIDATION
In a large cohort of patients

STAGE 04 — REGULATORY QUALIFICATION
Complex process supported by regulatory agency guidance

USES OF POTENTIAL BIOMARKERS IDENTIFIED IN AD

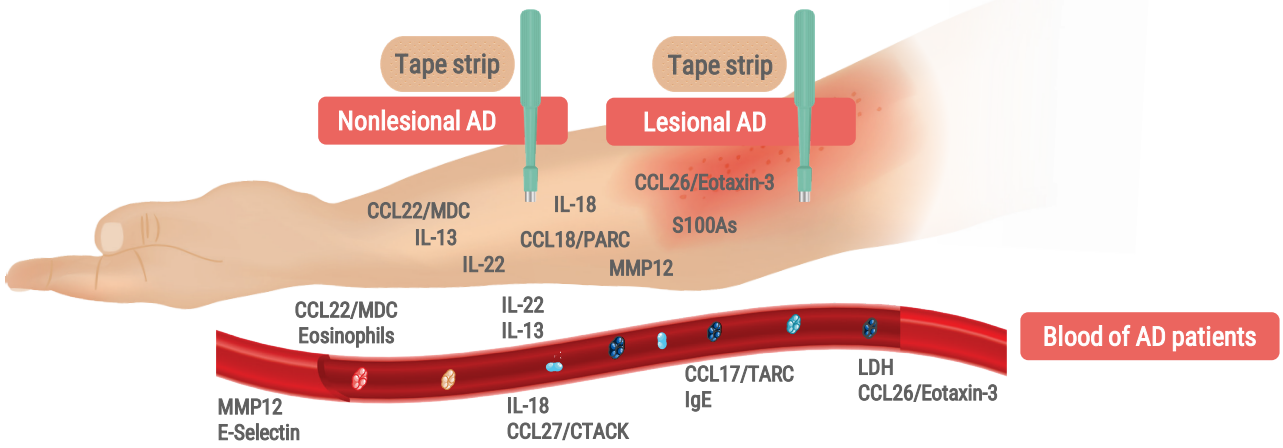
01 — IMPROVE DIAGNOSIS
Eg: differentiate AD and psoriasis

02 — REFLECT DISEASE SEVERITY
Eg: monitor treatment efficacy and motivate patient adherence

03 — PREDICT ONSET
Eg: intervene early in high-risk neonates

04 — PREDICT RESPONSE
Eg: disease-response and treatment-specific biomarkers guide treatment

POTENTIAL BIOMARKERS FOR AD IN NONLESIONAL AND LESIONAL AD SKIN AND BLOOD



AD BIOMARKERS ACROSS DISEASE PHENOTYPES

T_H2 and T_H22 pathways commonly activated across AD subtypes, but specific biomarkers vary among different populations.

01 — DIFFERENT ETHNICITIES
Eg: Asian biomarkers correlate with clinical phenotype: psoriasiform type lesions

02 — AD COMORBIDITIES
Eg: biomarkers may reflect AD clinical severity and predict food allergy

03 — AGE-RELATED CHANGES
Eg: elderly biomarkers reflect ↓ barrier defect; infant biomarkers similar to psoriasis

04 — *S aureus* COLONIZATION
Higher levels of type 2 biomarkers and more severe clinical parameters

SAMPLES/TECHNIQUES FOR STUDYING AD BIOMARKERS

Blood	Relatively easy collection May more objectively represent overall skin involvement	Changes may be subtle and/or take longer to occur Some key biomarkers in skin not well detected (ie, CCL26/eotaxin-3)
Skin biopsy	High detection rates Locate barrier-related changes at specific areas Immunohistochemistry studies reveal structural changes	Painful and scarring Potential infections and poor healing
Tape strip	Minimally invasive and nonscarring Variable detection rate (50-100%) across studies Capture barrier-related changes in early disease	Tissue processing is time-consuming/technically challenging Cannot capture differences in skin depth, location of biomarkers, and structural changes

CONCLUSIONS

The potential of biomarkers in AD is yet to be fully elucidated. The review found that the chemokine with the greatest evidence-based support to become a potential AD biomarker, at both baseline and following therapy, is CCL17/TARC, a chemoattractant of T_H2 cells. Studies using more minimally invasive techniques, such as tape-strips, in which biomarker dynamics are closely monitored in relation to therapeutic response are needed to improve the validity and relevance of biomarkers in AD.

Abbreviations: AD=atopic dermatitis, CCL=chemokine C-C motif ligand, CTACK=cutaneous T-cell-attracting chemokine, EMA=European Medicines Agency, FDA=Food and Drug Administration, Ig=immunoglobulin, IL=interleukin, LDH=lactate dehydrogenase, MDC=macrophage-derived chemokine, MMP=metalloproteinase, PARC=pulmonary and activation-regulated chemokine, TARC=thymus and activation-regulated chemokine

Renert-Yuval Y, Thyssen JP, Bissonnette R, Bieber T, Kabashima K, Hijnen D, Guttman-Yassky E. Biomarkers in atopic dermatitis—a review on behalf of the International Eczema Council. *J Allergy Clin Immunol.* 2021. Online ahead of print. DOI: https://doi.org/10.1016/j.jaci.2021.01.013