

Clinical and molecular changes in pediatric patients with atopic dermatitis treated with dupilumab: an analysis from the TREATkids registry

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Meeting of the ADF Working Groups: *Atopic Dermatitis and Skin Barrier*

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Sponsoring Statement

TREATgermany is an academic, investigator-initiated clinical disease registry that is financially supported by AbbVie Deutschland GmbH & Co. KG, Almirall Hermal GmbH, Galderma S.A., LEO Pharma GmbH, and Sanofi. The TREATkids part of the registry is supported by Sanofi exclusively. The funders had no influence on the study design, data analysis or interpretation.

Background & Objectives

Atopic dermatitis (AD) in pediatric patients:

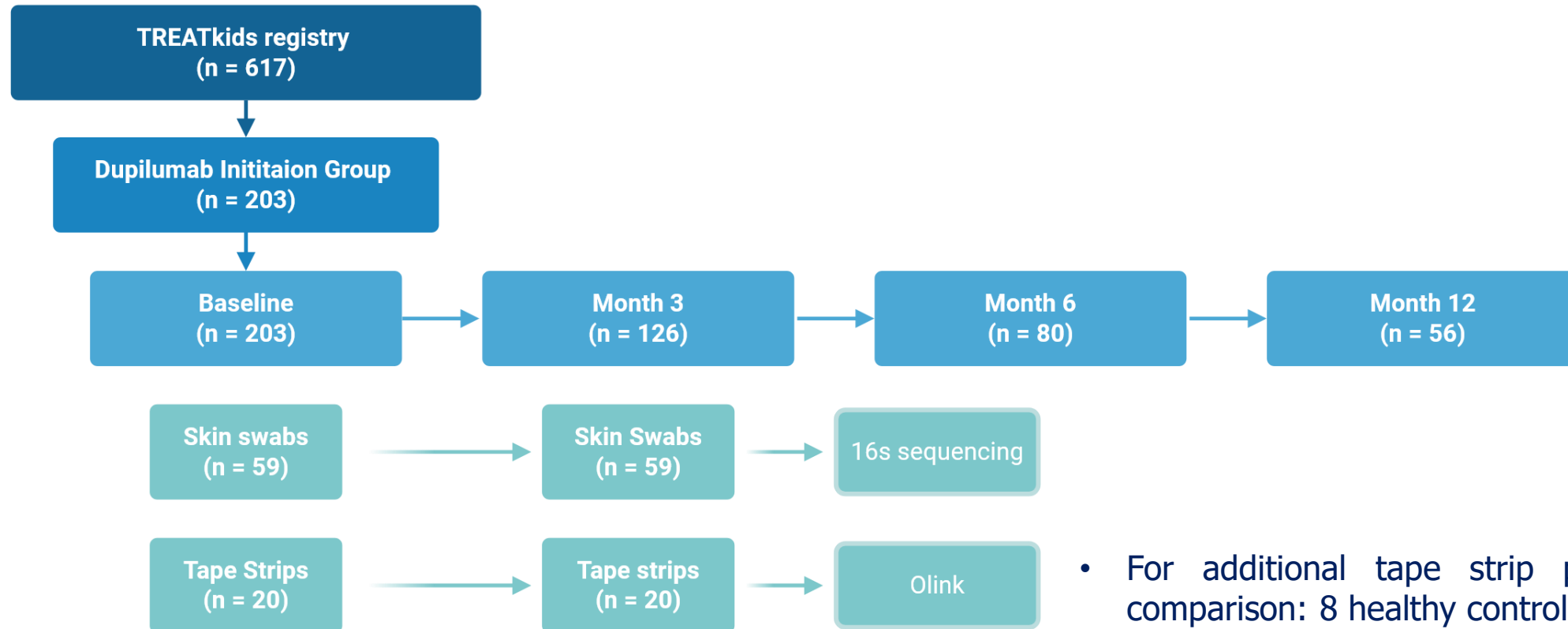
- Real-world effectiveness and long-term molecular outcomes of dupilumab remain insufficiently characterized
- Integrated clinical and molecular response data in pediatric routine care are limited

Objectives:

- To evaluate the real-world effectiveness of dupilumab in a pediatric population with atopic dermatitis
- To characterize treatment-associated changes in the skin proteome using tape-strip–based epidermal profiling
- To investigate the impact of dupilumab therapy on the cutaneous microbiome

Study Population & Methods

- **TREATkids:**
 - Prospective real-world pediatric cohort, part of TREATgermany registry
- **Study Population:** children and adolescents with moderate-to-severe AD

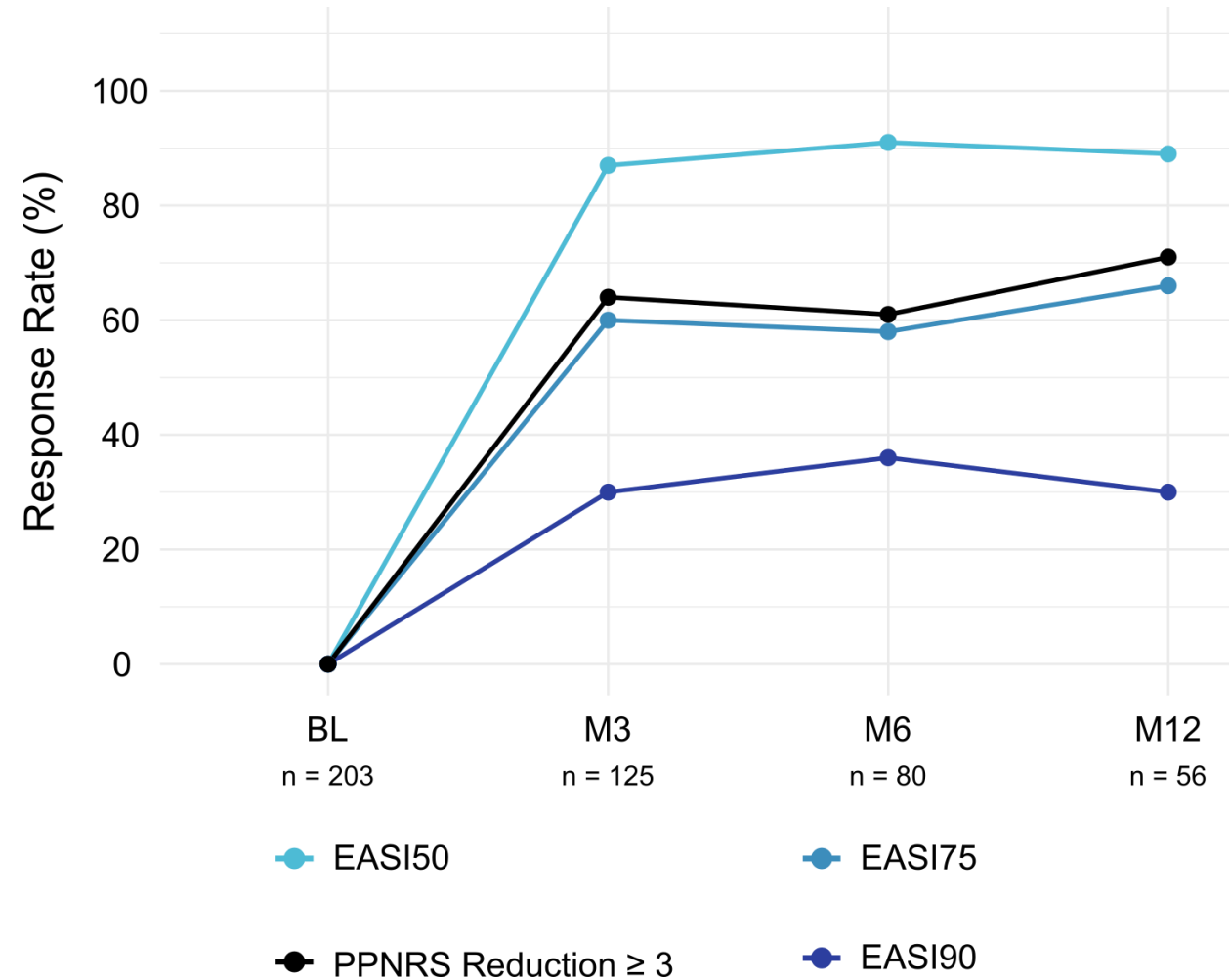


Sustained clinical response in pediatric real-world AD

Baseline characteristics

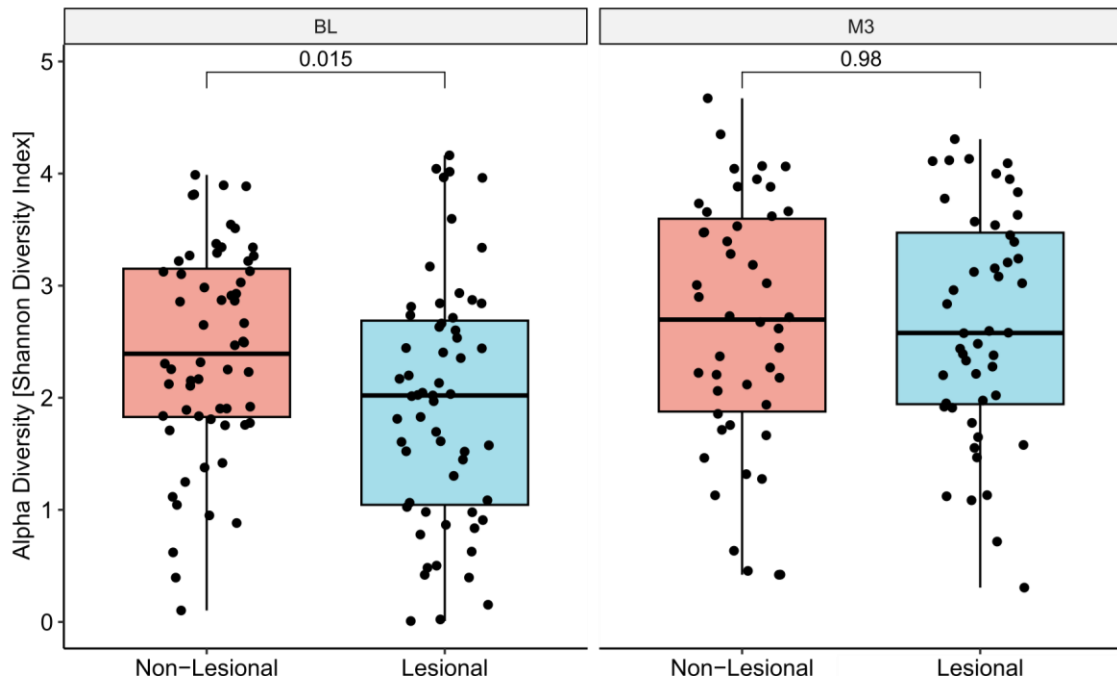
Variable	Total Patients	Dupilumab Initiation
Number of patients	617	203
Mean age (years)	7.5 ± 5.3	8.5 ± 5.1
Proportion with early onset (≤ 2)	93.80 %	94.59 %
Female	301 (48.6%)	104 (51.2%)
Asthma	20.5 %	15.8 %
Rhinitis	40.4 %	35.0 %
IGA 3	39.1 %	38.38 %
IGA 4	30.5 %	50.81 %
IGA 5	6.3 %	10.81 %
Mean PtGA	3.1 ± 1.1	3.6 ± 0.9
Mean EASI	12.1 ± 9.6	16.4 ± 9.0
Mean oSCORAD	36.8 ± 15.3	44.7 ± 12.3
Mean (C)DLQI	21.0 ± 6.5	18.6 ± 6.1
Mean Peak Pruritus (PP-NRS)	5.4 ± 2.9	6.5 ± 2.6
Mean number of Well Controlled Weeks (WCW)	4.2 ± 3.5	3.1 ± 3.0

Clinical effectiveness



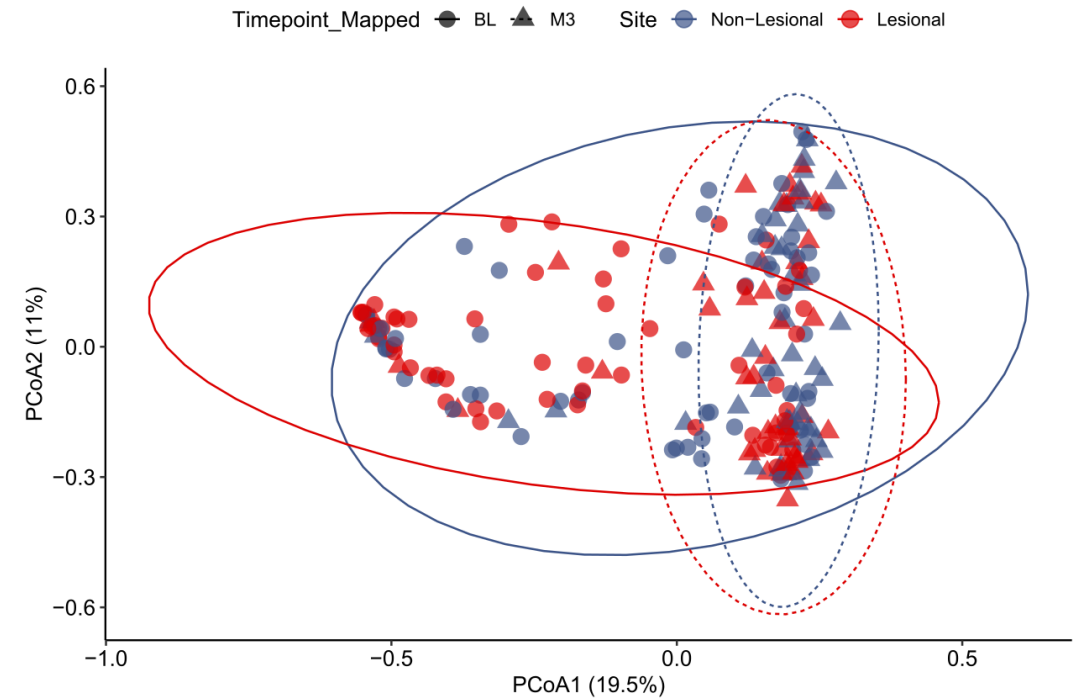
Microbial dysbiosis improves under treatment

α -diversity in lesional and non lesional skin



- Reduced α -diversity in lesional skin at BL ($p = 0.015$)
- Diversity normalizes at M3 ($p = 0.98$)

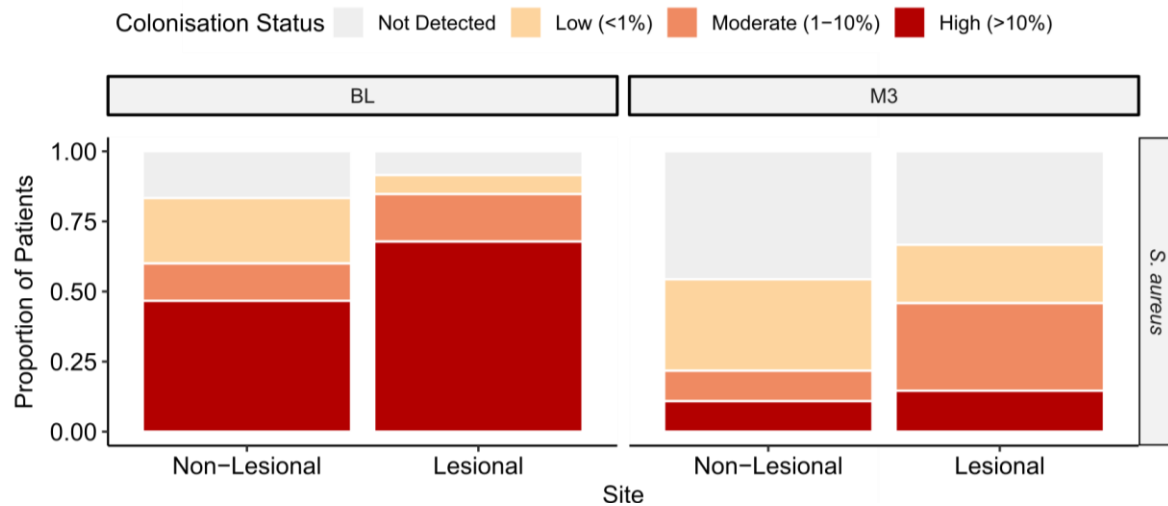
β -diversity in lesional and non lesional skin



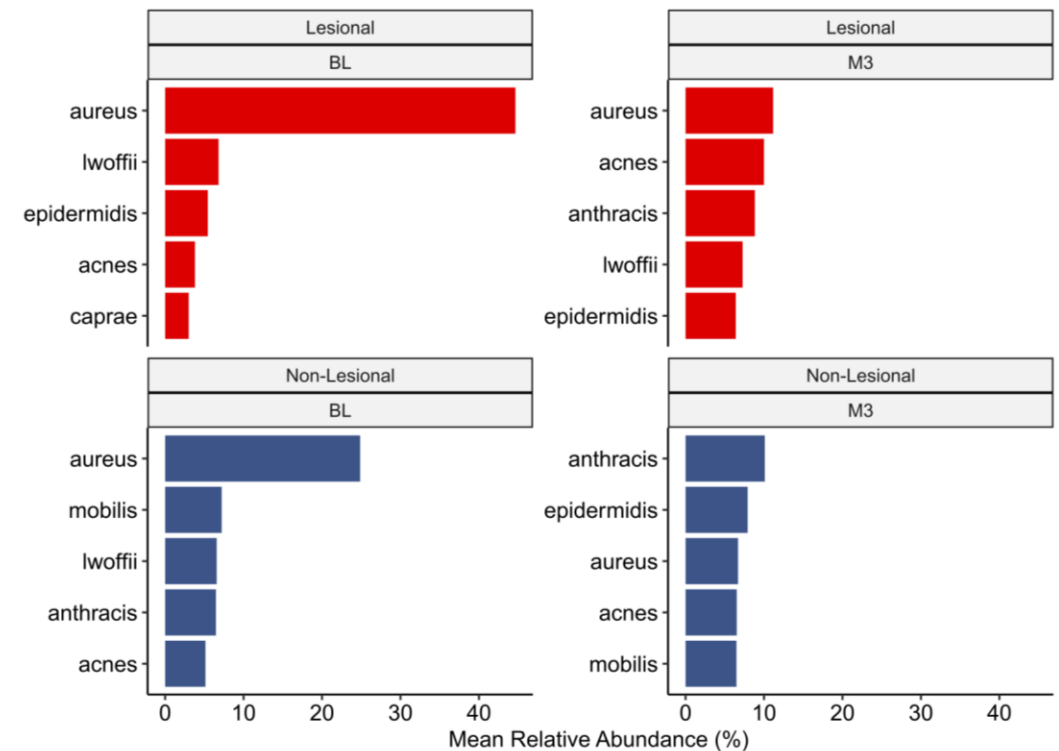
- Baseline lesional skin clusters separately ($p = 0.0013$), consistent with disease-associated dysbiosis
- M3 lesional cluster shifts toward non lesional

Treatment reshapes lesional microbial community structure

Distribution of *S. aureus* colonization



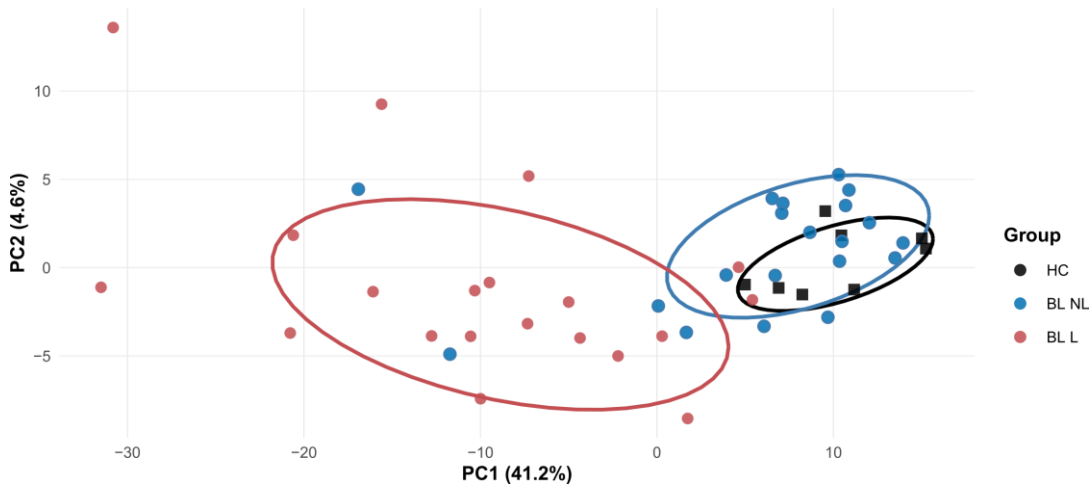
Mean relative abundance of the five most abundant bacterial species



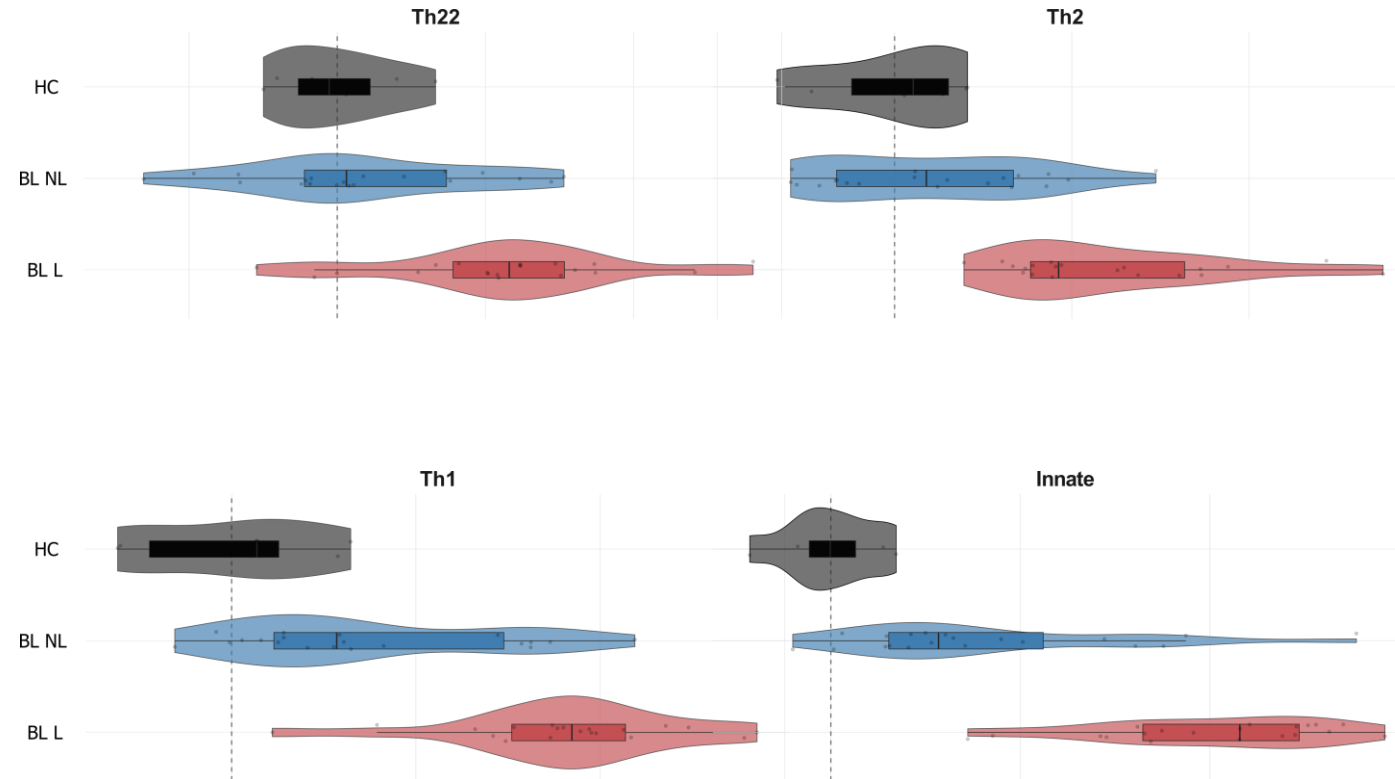
- High *S. aureus* colonization markedly reduced by month 3
- Relative expansion of commensal species (e.g., *C. acnes*, *S. epidermidis*)
- Consistent with normalization of skin microbiome under IL-4/IL-13 blockade

Baseline proteomic landscape in pediatric AD

Global proteomic separation at baseline



Inflammatory module activation in lesional skin



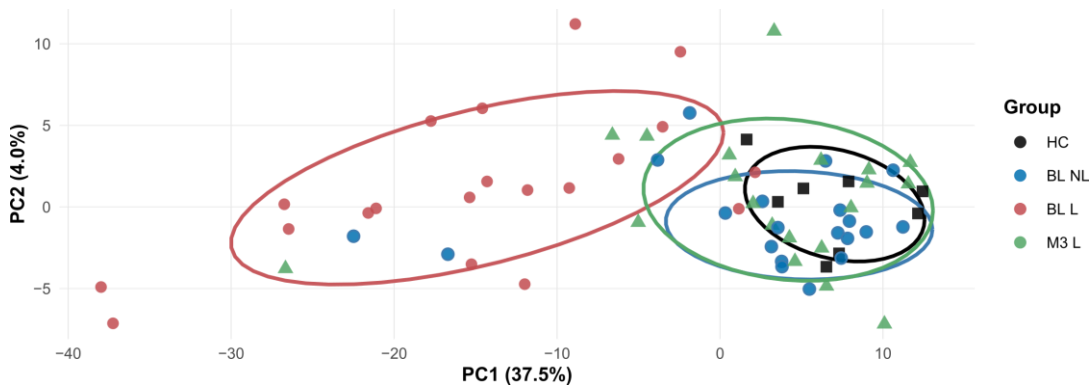
→ 161/360 proteins dysregulated (FDR<0.05; FC≥2)

→ Activation of adaptive and innate pathways

Distribution plots of HC-standardized module z-scores depict pathway activity across groups at the subject level.

Broad proteomic normalization in lesional skin by month 3

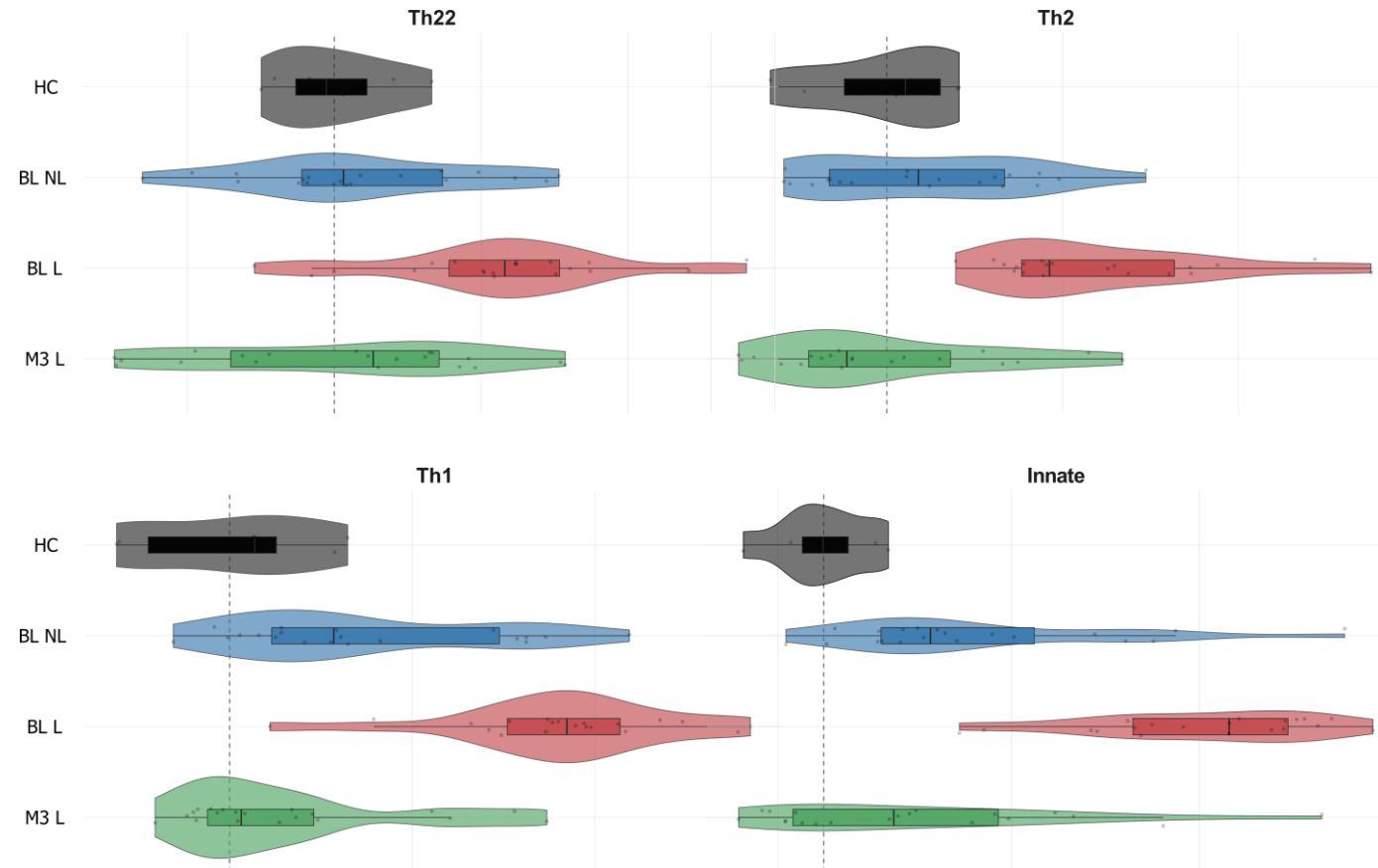
Global shift towards non lesional cluster



→ 159 proteins decreased at M3; 144 biologically relevant ($FC \geq 2$)

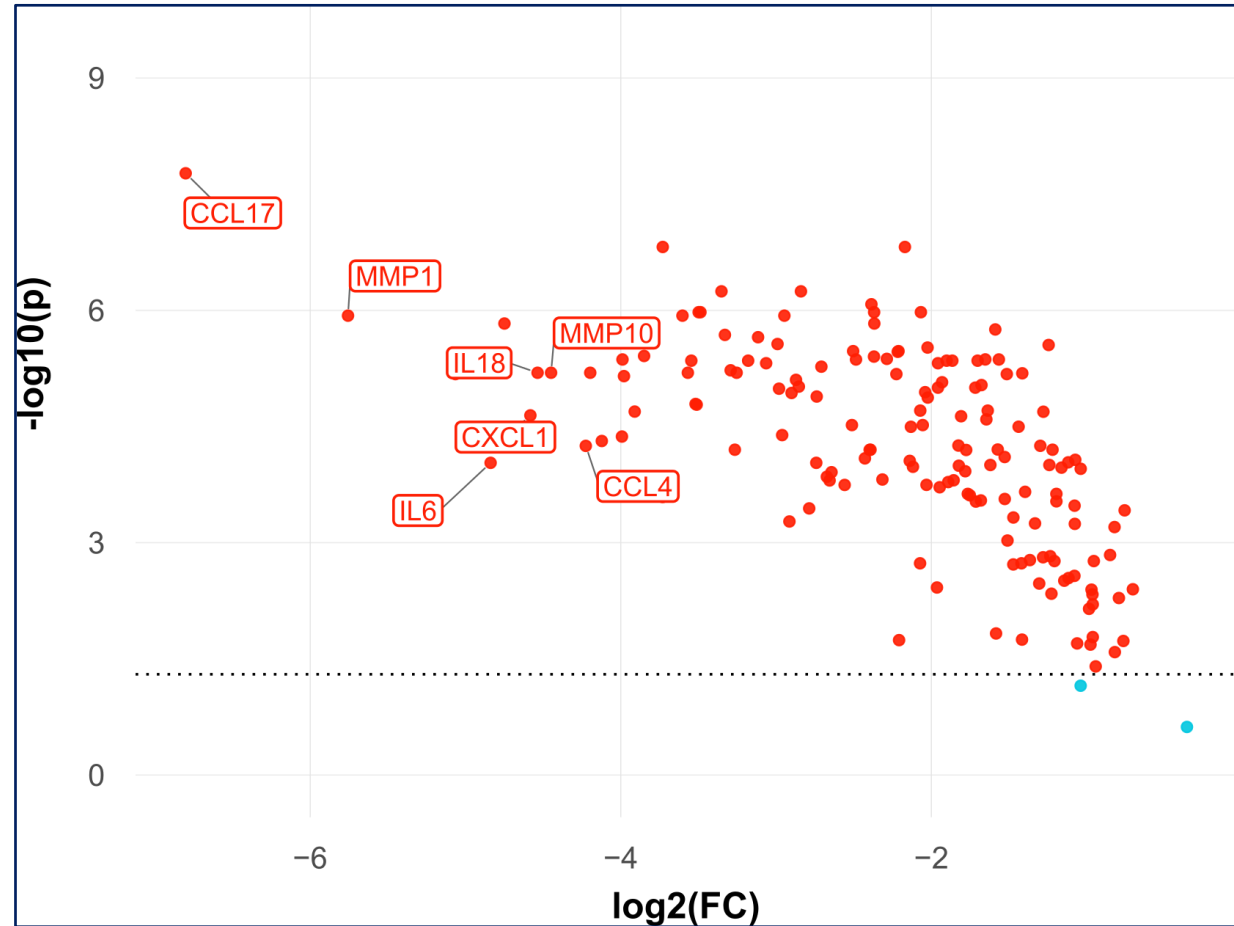
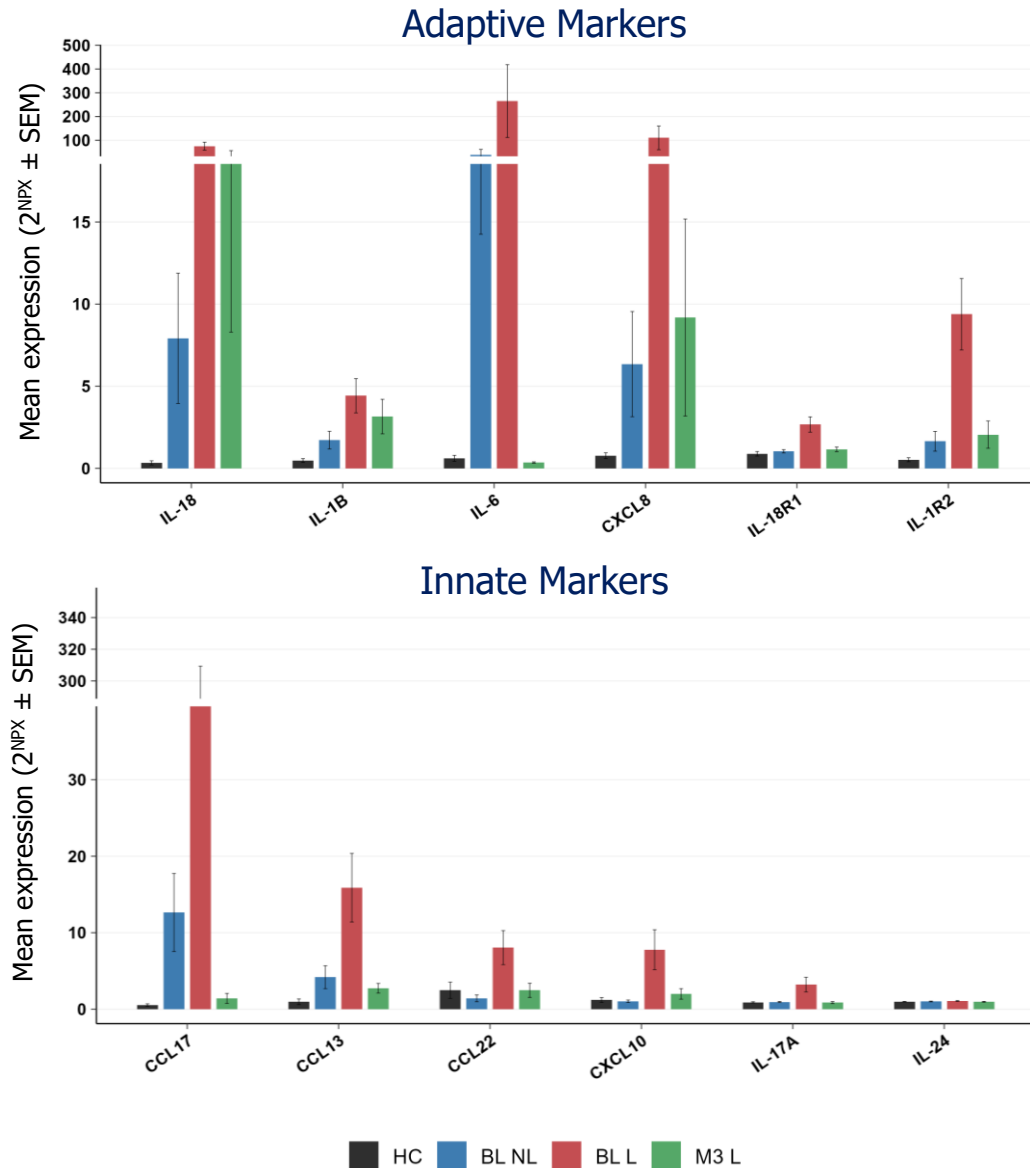
→ Restoration of lesional skin molecular profile toward non lesional state

Normalization of module activity throughout dupilumab treatment



Distribution plots of HC-standardized module z-scores depict pathway activity across groups at the subject level.

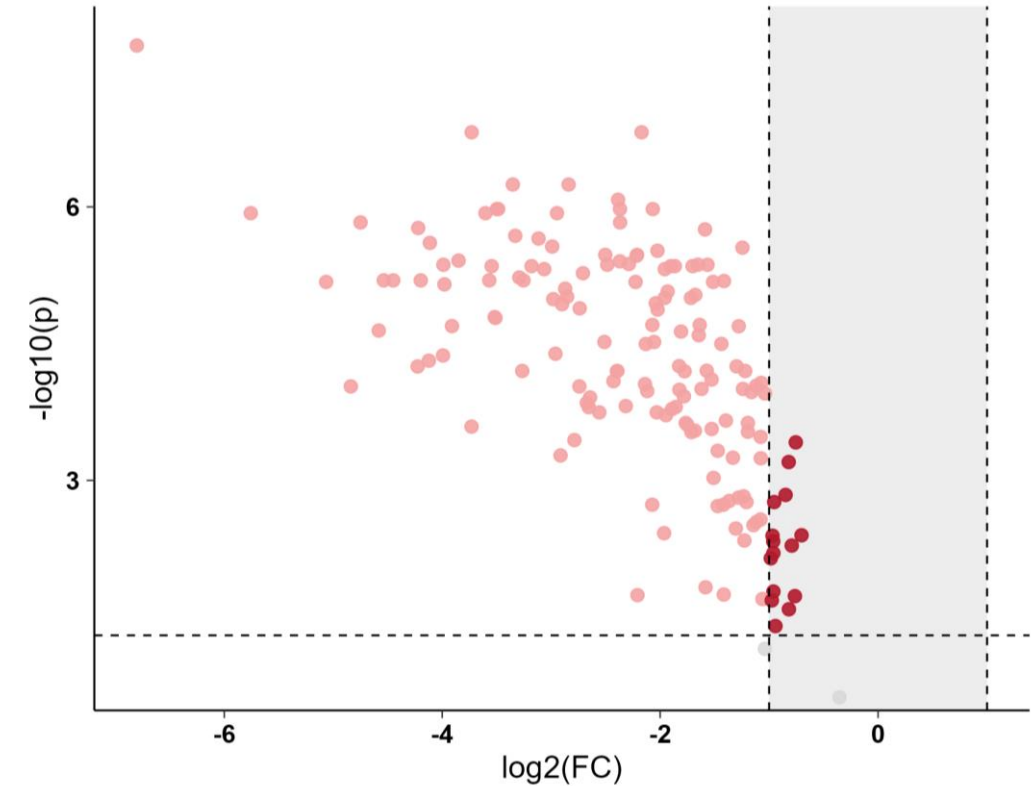
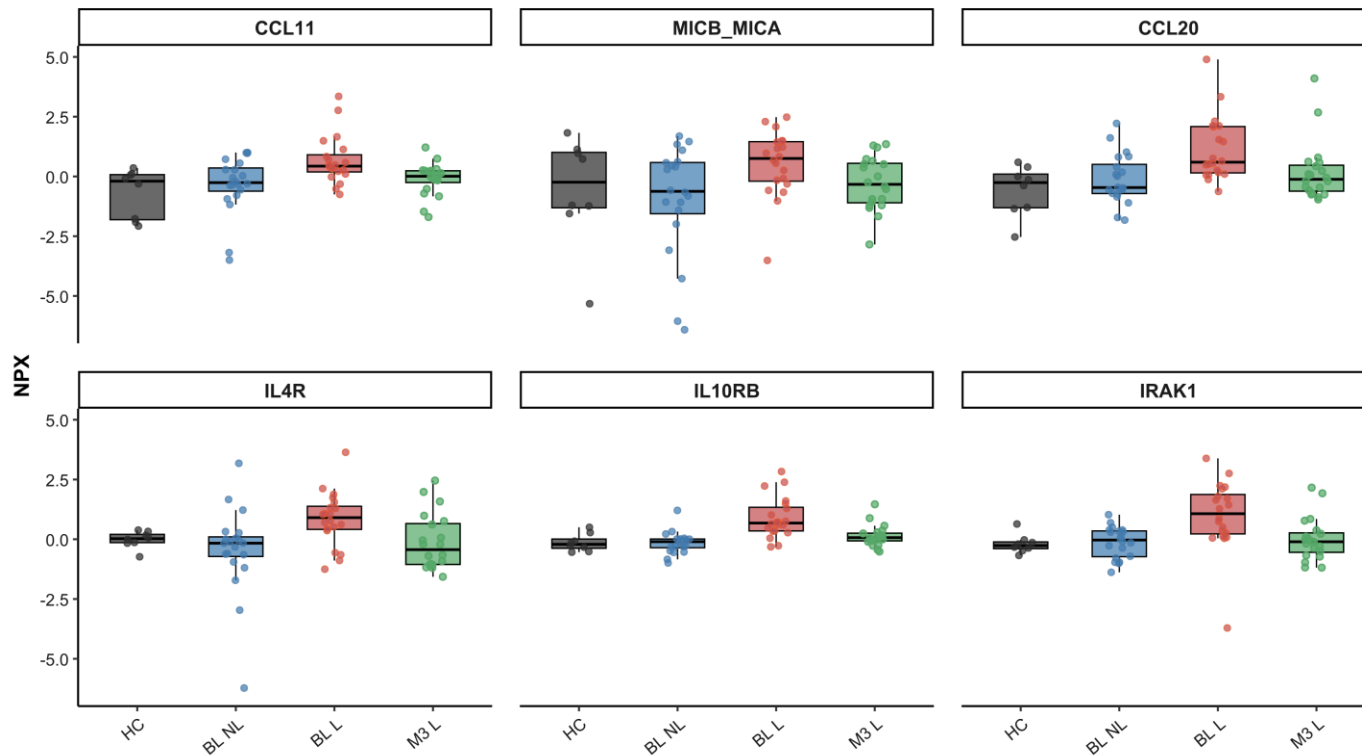
Key adaptive and innate mediators suppressed under treatment



Linear mixed-effects model (time point, lesion status; random intercept: patient); Benjamini–Hochberg correction). Red dots = $\text{FDR} < 0.05$

Incomplete molecular normalization under dupilumab therapy

Representative residual proteins



- 17 proteins did not reach the predefined biological relevance threshold
- Residual inflammatory protein expression under dupilumab therapy

Linear mixed-effects model (time point, lesion status; random intercept: patient); Benjamini–Hochberg correction), shaded area indicates $\log_2\text{FC} < 1$.

Conclusion

1. Dupilumab treatment shows robust effectiveness in pediatric AD
2. Minimally invasive tape-strip proteomics enables monitoring of molecular treatment response
3. Longitudinal microbial and proteomic profiling demonstrate intense reduction of dysbiosis and inflammation
4. At month 3, several protein biomarker and microbial features had not yet fully normalized to non-lesional levels, possibly reflecting residual pathways not fully modulated by dupilumab and/or the early sampling timepoint
5. Additional independent replication and further evaluation of biomarker panels are needed

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The members of the TREATgermany Study Group are listed on our registry website:

