



ASDP 62nd
Annual Meeting #ASDP25

November 6-9, 2025
Hilton Baltimore Inner Harbor **Baltimore, MD, USA**



Baseline skin cytokine and NOS2 profiles determined by RNA in situ hybridization correlate with response to anti-IL17 pathway biological therapies in patients with psoriasis

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1



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Disclosures

Category 1 (<\$10,000/last 24 mo)

Dr. William Damsky: Consultant/research funding, TWI Biotechnology; not ongoing.

The remaining collaborators have no relevant disclosures.

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2



Who will benefit from biological therapies?

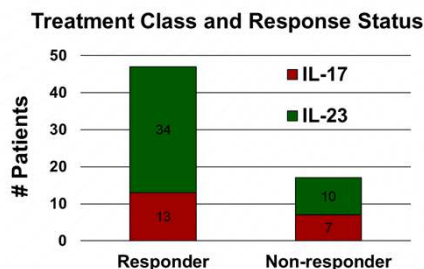
- Some patient characteristics (smoking, BMI, sex, comorbidities) are associated with treatment failure
- Attempts at prediction:
 - Genetic markers (HLA typing, TNF polymorphisms) → non-specific, expensive
 - Serum markers (CRP, ESR, C3, interleukins) → non-specific
 - Tissue tests:
 - Gene expression profiling: Expensive, not yet easily scalable
 - **NOS2**: Favors psoriasis over eczema; **IL13**: Favors eczema over psoriasis
 - IHC such as IL-36: Not yet routinely available, further studies needed

- Wang A, Fogel AL, Murphy MJ, et al. Cytokine RNA In Situ Hybridization Permits Individualized Molecular Phenotyping in Biopsies of Psoriasis and Atopic Dermatitis. *JID Innov.* 2021;1(2):100021.
- Garzorz-Stark N, Krause L, Lauffer F, et al. A novel molecular disease classifier for psoriasis and eczema. *Exp Dermatol.* 2016;25(10):767-774.
- Köhler I, Bivik Eding C, Kasic NK, Verma D, Enerbäck C. NOS2-derived low levels of NO drive psoriasis pathogenesis. *Cell Death Dis.* 2024;15(6):449.
- Zhang WR, Bhutani T, North JP. The Association of Interleukin-36 Staining Intensity and Response to Biologic Therapy in Patients With Psoriasis: A Retrospective Immunohistochemical and Chart Review Pilot Study. *J Cutan Pathol.* 2025;52(1):48-53.

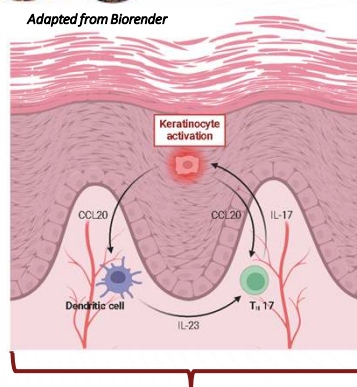
5

Study Design

- **Goal:** Determine if **pre-treatment biopsies** can predict biological therapies response
- Multi-institutional retrospective chart and histopathologic review
- **64 patients** met inclusion criteria
- Response: Body surface area



Adapted from Biorender



Surface: Intracorneal neutrophils, hyperkeratosis, parakeratosis, serum crust

Epidermal: Acanthosis, hypogranulosis, intraepidermal neutrophils and lymphocytes, mitoses, apoptotic keratinocytes, spongiosis

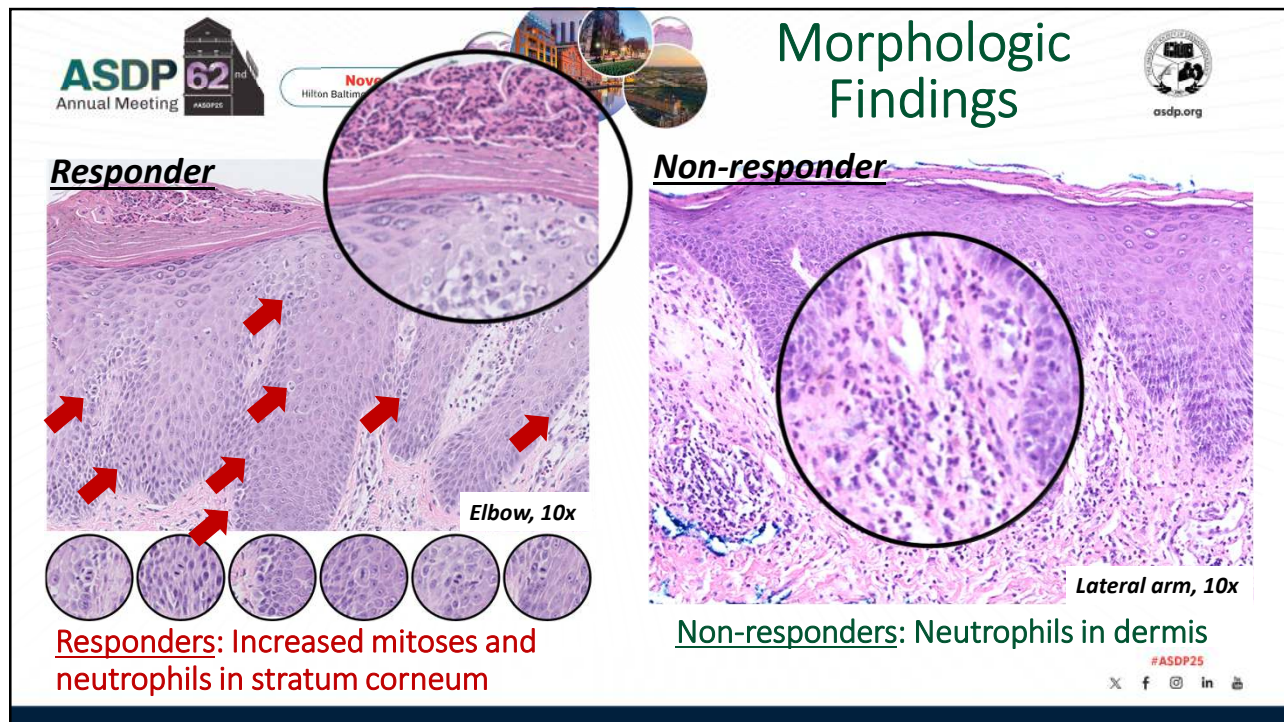
Dermal: Suprapapillary plate thinning, vascular dilation, dermal edema, RBC extravasation, immune milieu

Semiquantitative feature scoring (absent, +, ++) of surface, epidermal, and dermal histopathologic features

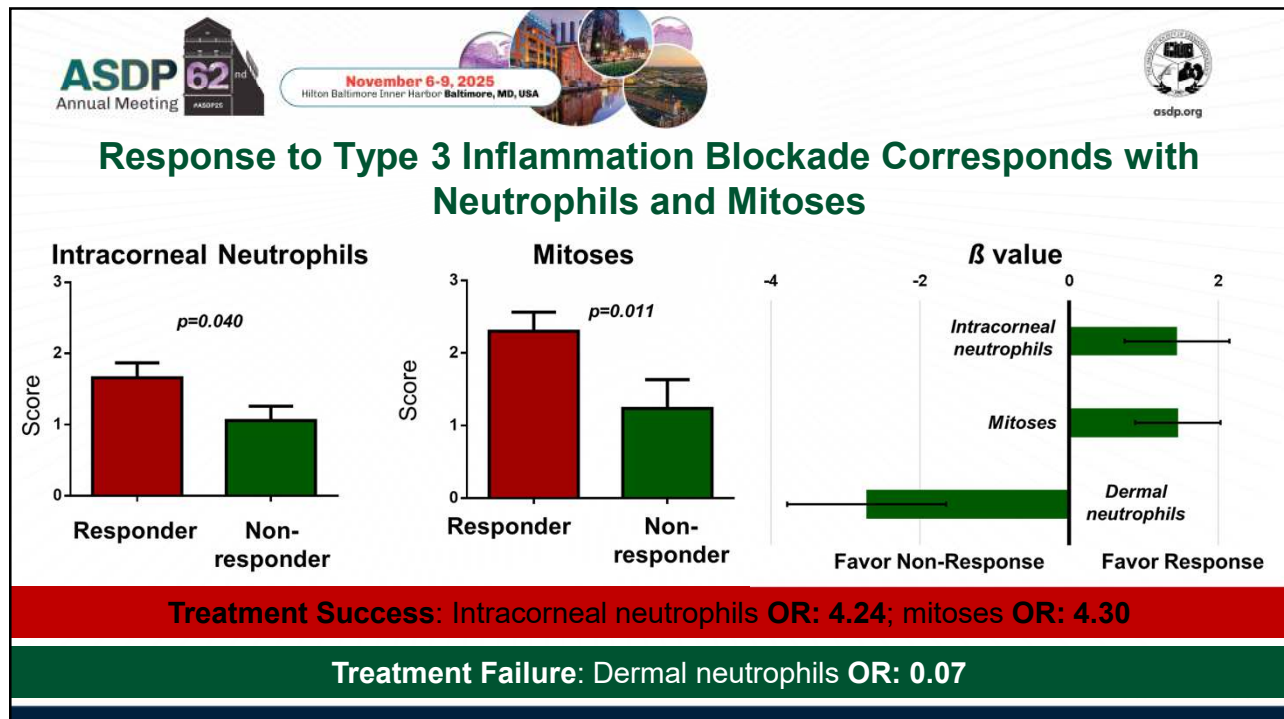
Singh, Katelyn et al. "Baseline skin cytokine profiles determined by RNA in situ hybridization correlate with response to dupilumab in patients with eczematous dermatitis." *Journal of the American Academy of Dermatology* vol. 88,5 (2023): 1094-1100.

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6



7



8

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RNA ISH Staining Quantification

0 1+ 2+ 3+ 4+

- No staining
- 1-2 dots/cell
- 3-10 dots/cell
- ≥ 10 dots/cell
- Dot clusters fill cytoplasm

• Dots often blurry
• Unclear relevance
• Likely background

• +/- small dot clusters
• Prominent dot clusters
• Cell obscured by stain

Increasing biologic significance

- Singh K, Valido K, Swallow M, et al. Baseline skin cytokine profiles determined by RNA in situ hybridization correlate with response to dupilumab in patients with eczematous dermatitis. *J Am Acad Dermatol.* 2023;88(5):1094-1100.
- Wang A, Fogel AL, Murphy MJ, et al. Cytokine RNA In Situ Hybridization Permits Individualized Molecular Phenotyping in Biopsies of Psoriasis and Atopic Dermatitis. *JID Innov.* 2021;1(2):100021.

9

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IL-17 Subset

NOS2

Score

Responder Non-responder

$p=0.0362$

IL17A

WCCS

Responder Non-responder

$p=0.203$

IL17F

WCCS

Responder Non-responder

$p=0.3643$

IL13

WCCS

Responder Non-responder

$p=0.2118$

- Cohort of 17 patients treated with IL-17 blockade (12 responders and 5 non-responders)
- NOS2 significantly elevated in non-responders

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10



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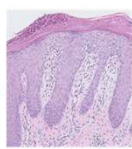
- **Proof of concept/pilot study: Pre-treatment RNA-ISH and H&E have predictive power for biologic therapy response in psoriasis**
 - **Responders:** Increased intracorneal neutrophils and mitoses, tend to have higher IL-17 by RISH
 - **Non-responders:** Increased dermal neutrophils, increased NOS2 by RISH
- Limitations
 - Retrospective design
 - Mixed therapy cohort
 - Varying pre-biologic treatment regimens



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Plaque
Psoriasis

Topical/oral
therapy trial

Biopsy

- H&E Evaluation
- RNA ISH

Biologically-informed choice of targeted therapy

11



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References

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12