backbones, future evaluations should also include domain-specialized models fine tuned for dermatology-relevant tasks, for example, MONET for dermatology image captioning (Kim et al, 2024). The open-source nature of these models confers key advantages, including greater transparency, flexibility, and control over data privacy and security—critical considerations for clinical deployment.

In conclusion, although general-purpose multimodal LLMs, such as ChatGPT, offer promising opportunities for dermatologic image analysis, their baseline performance remains limited. Methodological enhancements—such as few-shot learning, retrieval-augmented generation, and multiagent systems—have shown clear benefits but often at the cost of accessibility. Advancing the responsible use of these models requires both broader and deeper evaluation: broader, to encompass both closed- and open-source general-purpose models as well as their variants fine tuned for specific dermatology tasks; deeper, to rigorously assess diagnostic accuracy alongside explanation quality and reasoning fidelity. Such comprehensive evaluation represents a critical step toward trustworthy and clinically meaningful adoption of multimodal LLMs in dermatology.

Additional supporting details to the discussed limitations are described in Supplementary Materials and Methods.

ETHICS STATEMENT

This work was based on reviewing published papers. Because the work is classified as not-human-subjects research, review of the Institutional Review Board of West Virginia University was not required.

DATA AVAILABILITY STATEMENT

No new dataset was generated from the work.

KEYWORDS

Dermatologic images; Diagnosis; Explainability; Multimodal large language models; Trustworthy AI

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CONFLICT OF INTEREST

The authors state no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: GH; Formal Analysis; LK, GH; Funding Acquisition: GH; Supervision; GH; Writing – Original Draft Preparation: GH; Writing – Review and Editing: LK, GH

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2025.05.015.

REFERENCES

Akuffo-Addo E, Samman L, Munawar L, Akbik M, Kokikian N, Wescott R, et al. Assessing GPT-4's diagnostic accuracy with darker skin tones: underperformance and implications. Clin Exp Dermatol 2024;49:1244–5.

Kim C, Gadgil SU, DeGrave AJ, Omiye JA, Cai ZR, Daneshjou R, et al. Transparent medical image AI via an image-text foundation model grounded in medical literature. Nat Med 2024;30:1154–65.

Mackenzie EM, Sanabria B, Tchack M, Khan S, Rao B. Investigating the diagnostic accuracy of GPT-4's novel image analytics feature in dermatology. J Eur Acad Dermatol Venereol 2024;38:e954–6.

Nielsen JPS, Grønhøj C, Skov L, Gyldenløve M. Usefulness of the large language model ChatGPT (GPT-4) as a diagnostic tool and information source in dermatology. JEADV Clin Pract 2024;3:1570–5.

Shifai N, van Doorn R, Malvehy J, Sangers TE. Can ChatGPT vision diagnose melanoma? An exploratory diagnostic accuracy study. J Am Acad Dermatol 2024;90:1057–9.

Smith L, Hanna R, Hatch L, Hanna K. Computer vision meets large language models: performance of ChatGPT 4.0 on dermatology boards-style practice questions. J Skin 2024;8:1815–21.

Vashisht P, Lodha A, Maddipatla M, Yao Z, Mitra A, Yang Z, et al. UMass-BioNLP at MEDIQA-M3G 2024: DermPrompt-A systematic exploration of prompt engineering with GPT-4V for dermatological diagnosis. In: Proceedings of the 6th clinical natural language processing workshop. Stroudsburg, PA: Association for Computational Linguistics; 2024. p. 502–25.

Wang J, Hu G. Boosting GPT-4V's accuracy in dermoscopic classification with few-shot learning. Comment on "can ChatGPT vision diagnose melanoma? An exploratory diagnostic accuracy study". J Am Acad Dermatol 2024;91:e165–6.

Wang J, Yu TC, Kolodney MS, Perrotta PL, Hu G. Adapting ChatGPT for color blindness in medical education. Ann Biomed Eng 2025a;53:5–8.

Wang J, Zinn Z, Xu D, Hu G. Limitations and risks of custom GPTs in dermatology. Comment on "ReconGPT: a novel artificial intelligence tool and its potential use in post-Mohs reconstructive decision-making". J Am Acad Dermatol 2025b;92:e161–2.

Epidermal IL-36 and CCL17 Protein Expression Distinguish Palmar Eczema from Palmar Psoriasis

JID Open

Journal of Investigative Dermatology (2025) **145,** 3188–3191; doi:10.1016/j.jid.2025.04.040

TO THE EDITOR

The diagnosis of atopic dermatitis (AD) and psoriasis is primarily based on clinical morphology and lesion-

Abbreviation: AD, atopic dermatitis; ROC, receiver operating characteristic

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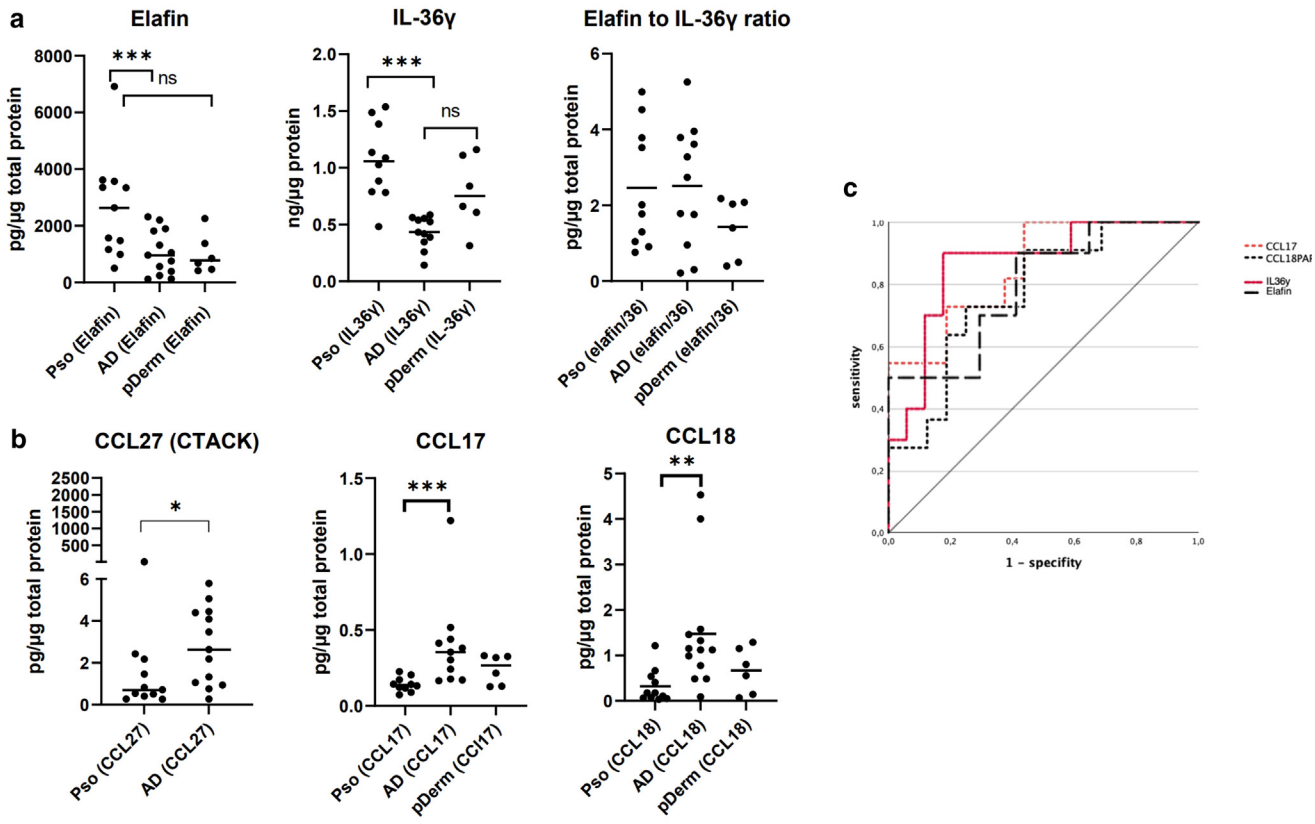

Figure 1. High CCL17 characterizes eczema, and high IL-36γ protein expression characterizes psoriatic inflammation of the palm. Proteins extracted from tape samples were measured by ELISA and normalized to total protein content in the sample. Kruskal–Wallis tests were conducted to examine differences for (**a**) elafin and IL-36γ and (**b**) CCL17 and CCL18 among AD, Pso, and pDerm. (**c**) ROC curves of the data indicate sensitivity and specificity for each significant marker. Area under the ROC curve values are 0.955 for IL-36γ, 0.773 for elafin, 0.927 for CCL17, and 0.845 for CCL18 to distinguish between AD and Pso. CCL27 proved significant when only AD and Pso groups were compared using Mann–Whitney U test (area under the curve in ROC analysis was 0.800). ***$P < .001$, **$P < .01$, and *$P < .05$. AD, atopic dermatitis; pDerm, psoriasiform dermatitis; Pso, psoriasis; ROC, receiver operating characteristic.

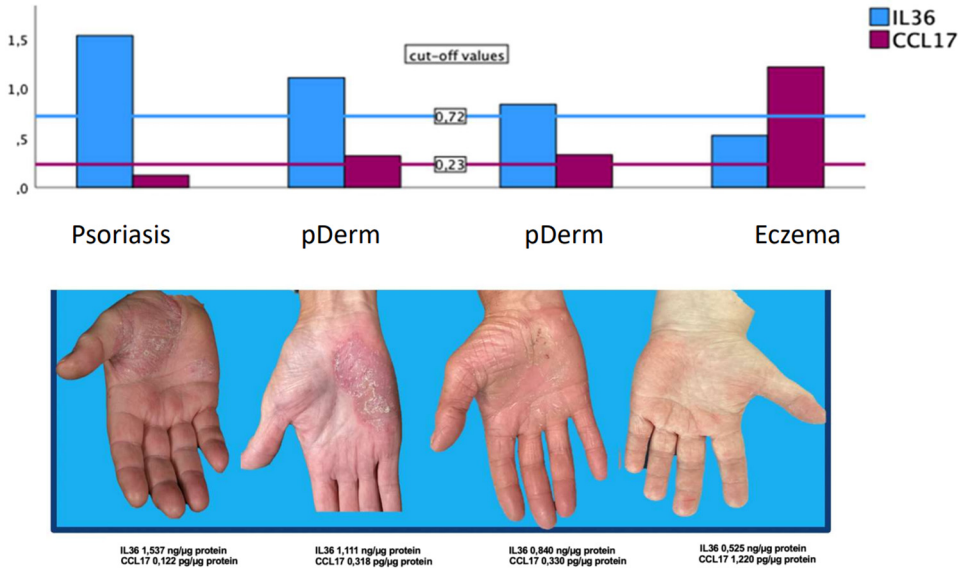

Figure 2. Clinical case examples of all phenotypes with corresponding CCL17 and IL-36 values. Y-axis = cut-off values as determined by ROC analysis for CCL17 (0.23, purple) and IL-36 (0.72, blue). X-axis = patient numbers with matching clinical pictures below. Patients gave informed written consent for their hand photographs to be published. ROC, receiver operating characteristic.

distribution patterns. However, even experienced physicians have difficulties in distinguishing between eczema and psoriasis, particularly in certain areas such as outer ear canal or palmoplantar regions. In this study, we have focussed on palmar skin manifestations. Although histopathology is considered state of the art for diagnosis, it has limitations. This is especially true for hyperkeratotic rhagadiform palmoplantar presentations and superinfected eczema because they can resemble psoriasiform changes in histology (An et al, 2020; Politiek et al, 2020). Thus, there exists no fully reliable diagnostic gold standard in clinical practice.

Epidermal sampling by tape stripping is a noninvasive method that can provide molecular information in skin diseases with epidermal involvement.

We enrolled 30 consecutive patients who all gave their written informed consent to participate in the study (ethical approval was obtained from Landesärztekammer Mainz [2022-16524]): 13 patients with known typical eczema lesions and distribution pattern on palmar sites, 11 with known plaque psoriasis showing pathognomonic lesions on the body as well as palmar involvement, and 6 patients with an unclear/overlap clinical phenotype (as evidenced by receiving different diagnoses by different dermatologists and/or therapy response failure to pathway-specific approaches) with only palmar involvement (Supplementary Table S1). Patients on immunosuppressant drugs within the past 12 weeks were excluded from the study. Patients had not used topical corticosteroids on the sampled area for at least the preceding 48 hours. Epidermal sampling was performed with D-Squame Discs (Clinical and Derm) as previously described (Berekmeri et al, 2024). Extracted protein content was measured by BCA (Life Technologies) and by ELISA (DuoSet for CCL27, CCL17, CCL18 and Elafin [RnD Systems]; high sensitivity iNOS [Biozol]) or multiplex measurement (Legendplex, BioLegend), and values obtained were normalized to total protein content.

On the basis of existing data (Berekméri et al, 2018; Berekmeri, 2024; D'Erme et al, 2015; Quaranta et al, 2014), selected proteins were determined in epidermal samples. Our results showed that for palmar lesions, IL-36γ proved to be more suitable to differentiate between psoriasis and eczema ($P < .001$) than elafin ($P = .03$) (Figure 1). The receiver operating characteristic (ROC) curve analysis showed a cut-off value of 0.7 ng/μg when 80% specificity was chosen. CCL17 showed a significantly higher expression in eczema ($P = .002$). The ROC curve analysis showed a cut-off level of 0.2 pg/μg protein for CCL17 when an 80% specificity was chosen (Figure 1). CCL18 was also found to distinguish AD from psoriasis, whereas CXCL1 (Groα) and inducible nitric oxide synthase proved unsuitable to differentiate AD from psoriasis in our proteomics dataset. Thus, in Mann–Whitney *U* test to compare epidermal samples between AD and psoriasis, there was a significant difference for IL-36γ ($P < .001$), CCL17 ($P < .001$), CCL18 ($P = .001$), elafin ($P = .011$), and CCL27 ($P = .035$) levels.

Regarding the unclear/overlap cases, those showed substantial expression of IL-36γ compared with our previously published analysis of healthy donor levels, which fell consistently below the range (100 pg/μg total protein) (Berekméri et al, 2018); relatively low expression of elafin; and moderate expression of CCL17 (Figures 1 and 2). Given the dominance of IL-36, we suggest to refer to this category affecting palmar sites as psoriasiform dermatitis instead of overlap dermatitis. Examples of morphologies shown by typical psoriasis, typical eczema, and psoriasiform dermatitis as well as their corresponding epidermal protein profiles are presented in Figure 2. It becomes clear that morphology alone is insufficient to inform on the underlying endotype.

Biomarkers found in skin biopsies RNA (Quaranta et al, 2014) and epidermal proteomics showed a clear difference, but both methods are effective in distinguishing between eczema and psoriasis. Of note, inducible nitric oxide synthase found at the mRNA level to be a psoriasis-specific marker (Quaranta et al, 2014) proved not useful when epidermal proteins were analyzed.

However, both approaches are in support of CCL17, CCL18, and CCL27 being useful to characterize eczema lesions. CCL17 attracts preferentially CCR4+T helper 2 cells. CCL18 binds to CCR8 and is known to be induced by IL-4 and IL-13 in epithelial cells.

Comparing epidermal proteomics results of the palmar lesional skin with published data on body skin lesions, we noticed the following differences: in palmar lesions, IL-36γ was superior as a biomarker for psoriasis to elafin, whereas the opposite was true for body skin psoriasis (Berekmeri et al, 2024). CXCL1 failed to show a significant difference between palmar eczema and palmar psoriasis in epidermal samples, which was also not in line with findings from body sites (Berekmeri et al, 2024; Eyerich et al, 2011). Interestingly, elafin, a neutrophil serine protease inhibitor, is upregulated by neutrophil-derived elastase (Reid et al, 1999). In case of diminished CXCL1 expression, less difference may exist between palmar eczema and palmar psoriasis regarding neutrophils infiltration. Indeed, whereas the ratio between elafin and IL-36γ appears to be stable across cases of eczema and psoriasis, this ratio seems decreased in unclear/overlap cases. The coexistence of AD and psoriasis has been described previously. The fact that IL-36γ is highly expressed may point to a "psoriasiform dermatitis" instead of a true overlap situation despite moderately increased CCL17. Our data further support the idea that a separate endotype exists for the palmar skin that is not psoriasis nor eczema and not due to predominance of IL-36γ over CCL17 and may be referred to as "psoriasiform dermatitis" but could well resemble the previously proposed "psoriasiform eczema" (Lauffer and Eyerich, 2023).

Disease classification is of high clinical interest to facilitate patient stratification and choice of therapy. Further endotype characterization may suggest a pathway-specific approach for the palmar psoriasiform dermatitis subtype. Molecular diagnostics would be valuable as a point-of-care standard in clinically unclear cases and will support individualized treatment strategies.

DATA AVAILABILITY STATEMENT

Original data are available from the corresponding author upon request.

KEYWORDS

Endotype; Hand eczema; Overlap dermatitis; Palmoplantar; Psoriasis; Tape stripping

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CONFLICT OF INTEREST

The authors state no conflcit of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2025.04.040.

REFERENCES

An MK, Yoon JH, Park EJ, Park HR, Kim KJ, Kim KH. Differential histopathological and immunohistochemical findings between palmar psoriasis and chronic hand eczema. Eur J Dermatol 2020;30:710−5.

Berekméri A, Latzko A, Alase A, Macleod T, Ainscough JS, Laws P, et al. Detection of IL-36γ through noninvasive tape stripping reliably discriminates psoriasis from atopic eczema. J Allergy Clin Immunol 2018;142:988−91.e4.

Berekmeri A, Macleod T, Hyde I, Ojak GJ, Mann C, Kramer D, et al. Epidermal proteomics demonstrates elafin as a psoriasis-specific biomarker and highlights increased anti-inflammatory activity around psoriatic plaques [e-pub ahead of print]. J Eur Acad Dermatol Venereol 2024; https://doi.org/10.1111/jdv.20289 (accessed August 19, 2024).

D'Erme AM, Wilsmann-Theis D, Wagenpfeil J, Hölzel M, Ferring-Schmitt S, Sternberg S, et al. IL-36γ (IL-1F9) is a biomarker for psoriasis skin lesions. J Invest Dermatol 2015;135:1025−32.

Eyerich S, Onken AT, Weidinger S, Franke A, Nasorri F, Pennino D, et al. Mutual antagonism of T cells causing psoriasis and atopic eczema. N Engl J Med 2011;365:231−8.

Lauffer F, Eyerich K. Eczematized psoriasis - a frequent but often neglected variant of plaque psoriasis. J Dtsch Dermatol Ges 2023;21:445−53.

Politiek K, Loman L, Pas HH, Diercks GFH, Lemmink HH, Jan SZ, et al. Hyperkeratotic hand eczema: eczema or not? Contact Dermatitis 2020;83:196−205.

Quaranta M, Knapp B, Garzorz N, Mattii M, Pullabhatla V, Pennino D, et al. Intra-individual genome expression analysis reveals a specific molecular signature of psoriasis and eczema. Sci Transl Med 2014;6:244ra90.

Reid PT, Marsden ME, Cunningham GA, Haslett C, Sallenave JM. Human neutrophil elastase regulates the expression and secretion of elafin (elastase-specific inhibitor) in type II alveolar epithelial cells. FEBS Lett 1999;457:33−7.

Prevalence of Pyoderma Gangrenosum: A Systematic Review and Meta-Regression Analysis

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TO THE EDITOR

Pyoderma gangrenosum (PG) is a neutrophilic dermatosis that is characterized by ulcerations most often of the lower legs and is known to have various presentations, contributing to high rates of misdiagnosis in PG (George et al, 2019; Wollina, 2007). Misdiagnosis contributes to delays in proper treatment, causing complications, including delay in healing of ulcers, continued pain and activity of daily living impact, and increased costs (George et al, 2019; Haddadin et al, 2024).

PG is considered a rare disease, with very few estimates of prevalence in the general population existing in the current literature. One study conducted in the United States found that 0.0058% of the study population had PG (Xu et al, 2020). Prevalence has been estimated to be higher in certain subgroups, including those with PG-associated diseases, such as

Abbreviations: CD, Crohn's disease; CI, confidence interval; HS, hidradenitis suppurativa; IBD, inflammatory bowel disease; PG, pyoderma gangrenosum; RA, rheumatoid arthritis; UC, ulcerative colitis

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Supplementary Table S1. Descriptive Characteristics (Mean ± SD, Range) of the Studied Groups

Phenotype	Psoriasis	Eczema	Overlap Type
Total (n)	11	13	6
Female	7	10	2
Male	4	3	4
Age, y, mean ± SD	60 ± 9.2	51.3 ± 14.4	52.2 ± 16.2
Range	40–72	21–71	24–71
Disease duration, y, mean ± SD	5.6 ± 5.8	4.5 ± 5.3	7 ± 9.5
Range	0.2–17	1–21	2–24