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A Report from the 54th Annual European Society for Dermatological Research (ESDR) Meeting

Deepak Balak, MD, PhD, MSc, IPC Jr. Councilor

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS

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INTRODUCTION

The 54th Annual Meeting of the European Society for Dermatological Research (ESDR) was held in Antwerp, Belgium, from Wednesday, September 10 to Saturday, September 13, 2025. The event brought together more than 1,000 delegates, representing a diverse community of physicians and scientists from around the world, speaking over 30 languages. This report highlights the latest advancements in psoriasis research, summarizing key sessions from the meeting, including the IPC Symposium: Psoriasis—Differential Diagnosis, Paradoxical Responses, and New Treatment Mechanisms.

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Immune Shifts in Psoriasis

Michel Gilliet, MD, IPC Councilor
University of Lausanne, Lausanne, Switzerland

Professor Gilliet presented his translational work, which is focused on improving the diagnosis and treatment of psoriasis and other inflammatory skin diseases by identifying and applying immune modules. These modules are distinct gene expression profiles representing key immunological pathways, identified through transcriptomic profiling. Using these analyses, Professor Gilliet developed an immune map defining seven core immune modules: Th1, Th2, Th17, type I interferon, neutrophilic, macrophagic, and eosinophilic.[1]

Psoriasis patients can be classified into several endotypes based on the transcriptomic clustering. Chronic plaque psoriasis is associated with the Th17 module, acute inflammatory psoriasis with the type 1 interferon, and pustular forms of psoriasis with the neutrophilic module.

This endotype classification could help guide treatment choices. For instance, Th17-defined chronic plaque psoriasis can be treated with inhibitors of TNF, IL-23, IL-17/IL17R, and TYK2. Neutrophilic clustered psoriasis, which includes pustular forms such as GPP and PPP, can be treated with retinoids, methotrexate, apremilast, and inhibitors of IL-1R and IL-36R. Finally, treatment options for the type 1 interferon-defined psoriasis (acute psoriasis, meaning unstable, erythrodermic, and paradoxical cases) are cyclosporin, UV phototherapy, and TYK2 inhibitors.

Professor Gilliet also discussed cases of non-responders who exhibited immune shifts during treatment. For instance, dominant type I interferon activity was observed in patients who did not respond to Th17 blockade. Similarly, paradoxical reactions may result from immune shifts during targeted therapy (e.g., from Th17 to Th1 or Th2 modules). Adjusting treatment based on these shifts improved outcomes, thereby validating the immune module approach.

In summary, transcriptomic analyses enable the definition of specific psoriasis endotypes. While Th17 activity is a common feature across chronic plaque, other forms of psoriasis are linked to other immune modules. Identifying endotypes and recognizing immune shifts is therefore crucial for selecting appropriate therapies.[1]

Reference:

1. Immune Modules to Guide Diagnosis and Personalized Treatment of Inflammatory Skin Diseases. Seremet T, Di Domizio J, Girardin A, et al. *Nat Commun.* 2024 Dec 18;15(1):10688.

Where Does Psoriasis Fit into the Differential Diagnosis of Contact Dermatitis?

Julien Lambert, MD, PhD
University Hospital Antwerp, Antwerp, Belgium

Professor Julien Lambert discussed the clinical and immunological overlap between psoriasis and allergic contact dermatitis. While these are distinct conditions with different immune mechanisms, they share several features. Both diseases involve Th1 and Th17-mediated inflammation and skin barrier dysfunction, which may co-occur in the same patient. Clinically, dermatitis may koebnerize into psoriatic lesions. Histologically, mixed features of psoriasis and allergic contact dermatitis can be observed. This overlap can complicate the clinical distinction between psoriasis and allergic contact dermatitis.[1]

In particular, palmoplantar psoriasis can be challenging to differentiate from chronic hand dermatitis. A key example is hyperkeratotic hand eczema, which may show clinical and histopathological features resembling psoriasis. Moreover, biomarkers associated with the Th17 and IL-36 pathways are found in psoriasis and hand eczema. The term eczema in psoriasis describes a hybrid entity, typically in the presence of at least one relevant positive patch test. In such cases, a type IV contact allergy may contribute to psoriasiform palmoplantar disease that is not purely psoriatic. Therefore, patch testing is essential in the evaluation of chronic hand dermatitis.

It has been suggested that patients with moderate to severe or widespread psoriasis, including those with erythroderma, are less likely to develop allergic contact dermatitis. In contrast, allergic contact dermatitis is more frequently observed in patients with mild psoriasis, facial, nail, or palmoplantar involvement, and pustular psoriasis.[1]

Professor Lambert also outlined indications for patch testing in psoriasis patients. Patch testing should be considered in cases of:

- Therapy-recalcitrant disease
- Very localized psoriasis (e.g., on the thumb)
- Pustular psoriasis
- Atypical presentations, such as facial involvement, vesicular lesions, or intense pruritus
- Histopathological findings of eosinophilic infiltrates
- Co-existing dermatitis

Distinguishing psoriasis from allergic contact dermatitis can be challenging due to overlapping clinical and histological features. The term eczema in psoriasis is often used to describe this co-occurrence. Patch testing remains a critical diagnostic tool in complex or atypical cases.

Reference:

1. Differential Diagnosis of Contact Dermatitis: A Practical Approach Review by the EADV Task Force on Contact Dermatitis. Pesqué D, Aerts O, Bizjak M, et al. *J Eur Acad Dermatol Venereol.* 2024 Sep;38(9):1704-1722.

Paradoxical Psoriasis and Therapeutic Approaches

Paola Di Meglio, PhD, IPC Councilor
King's College London, London, United Kingdom

Professor Di Meglio gave an in-depth overview of paradoxical psoriasis induced by different targeted therapies, including TNF inhibitors, IL-17 inhibitors, and JAK inhibitors.[1] Paradoxical psoriasis is an umbrella term that encompasses two clinical scenarios: 1) cases of worsening of existing psoriasis in patients undergoing treatment with a targeted therapy; and 2) new onset psoriasiform reactions in patients treated with a targeted therapy for a different disease.

Paradoxical psoriasis is most commonly associated with TNF inhibitors, occurring in approximately 5% of treated patients. The underlying mechanism involves type I interferon overexpression, particularly in response to TNF blockade.[2] Among TNF inhibitors, infliximab is most frequently implicated. The condition is more prevalent in female patients, with a mean onset of 11 months (ranging from 1 month to several years). Clinical presentations include plaque and palmoplantar pustular psoriasis, though inverse, guttate, and generalized forms may also occur.

While paradoxical psoriasis often resolves after discontinuing the offending drug, it may persist in up to one-third of cases. Management depends on disease severity and control of the underlying condition. Topical or conventional systemic therapies may suffice for mild or localized disease with stable primary disease. For moderate to severe cases, a biologic switch is considered. IL-17 inhibitors are considered for patients without inflammatory bowel disease (IBD), especially with palmoplantar involvement. IL-12/23 or IL-23 inhibitors are an option for patients with IBD or mixed psoriasiform/eczematous phenotypes. JAK-1 inhibitors are a second-line option.

Paradoxical psoriasis has also been observed in atopic dermatitis patients treated with IL-4/IL-13 inhibitors, with a 1–2% incidence. These reactions are not yet well-standardized in terms of management. Options include topical therapies (e.g., vitamin D analogues + corticosteroids) and systemic treatments (e.g., UVB phototherapy, methotrexate, biologics). Switching therapies can also be considered, such as from IL-4/IL-13 blockade to IL-13-specific inhibitors or to JAK inhibitors, particularly JAK-1 or JAK-1/2 inhibitors.

Overall, paradoxical psoriasis represents a complex immune phenomenon triggered by targeted therapies. Its management requires individualized assessment, considering both the psoriasiform reaction and the underlying disease being treated.

References:

1. Paradoxical Psoriasis: An Updated Review of Clinical Features, Pathogenesis, and Treatment Options. Maronese CA, Valenti M, Moltrasio C, et al. *J Invest Dermatol.* 2024 Nov;144(11):2364-2376.
2. TNF Blockade Induces a Dysregulated Type I Interferon Response without Autoimmunity in Paradoxical Psoriasis. Conrad C, Di Domizio J, Mylonas A, et al. *Nat Commun*. 2018 Jan 2;9(1):25.

Drug-Induced Psoriasis

Deepak Balak, MD, PhD, MSc, IPC Jr. Councilor
Leiden University Medical Center, Leiden, The Netherlands

Dr. Balak provided a comprehensive overview of drug-induced psoriasis, a clinically relevant but often underrecognized phenomenon. Multiple medications have been implicated in either inducing de novo psoriasis or exacerbating pre-existing disease. However, robust evidence on specific drug associations remains limited.[1]

Classically, associated drugs in drug-induced psoriasis include beta-blockers, lithium, terbinafine, antimalarials such as hydroxychloroquine, and NSAIDs. The latency period varies by drug: < 4 weeks for terbinafine and NSAIDs, 4–12 weeks for antimalarials, and > 12 weeks for beta-blockers and lithium.[1] More recently, immune checkpoint inhibitors (ICIs) such as PD-1 inhibitors have been linked to new-onset psoriasis and existing disease flares, likely due to T cell overactivation. Onset typically occurs between 1 and 10 months, with earlier onset in exacerbation cases.

Diagnosing drug-induced psoriasis is challenging, as clinical and histopathological features often mirror idiopathic psoriasis. The latency period can range from weeks to years, and no standardized criteria exist to distinguish drug-induced from conventional psoriasis. The Naranjo Adverse Drug Reaction Probability Scale may aid in assessing causality.[2]

A broad spectrum of psoriasis phenotypes has been reported in drug-induced cases, including plaque, palmoplantar, scalp, pustular, and erythrodermic types. Morphological transformation (e.g., new pustular lesions in a patient with plaque psoriasis) has also been described. In addition, psoriasiform dermatitis, lacking classic psoriasis features like sharp demarcation or the candle-grease sign, has also been implicated in drug-related reactions.

Histopathological assessment may help diagnose drug-induced psoriasis, although histopathology alone cannot exclude a drug-related cause. Histopathological clues suggestive of a drug-related cause include absence of tortuous papillary dermal capillaries and suprapapillary thinning, low number of Munro microabscesses, presence of eosinophilic infiltrates, lichenoid inflammation, and spongiosis.

In summary, drug-induced psoriasis is often difficult to recognize, particularly in the context of polypharmacy and variable latency periods. Clinically, a psoriasis flare in the absence of other triggering factors should raise the possibility of a drug-related cause. A thorough medication review and multidisciplinary approach are essential for accurate diagnosis and optimal management.

References:

1. Drug-Induced Psoriasis: Clinical Perspectives. Balak DM, Hajdarbegovic E. *Psoriasis (Auckl).* 2017 Dec 7;7:87-94.
2. A method for estimating the probability of adverse drug reactions. Naranjo CA, Busto U, Sellers EM, et al. *Clin Pharmacol Ther*. 1981 Aug;30(2):239-45.

Mechanisms of Topical Drug Delivery: Opportunities for Psoriasis?

Robert Rissmann, PhD
Centre for Human Drug Research & Leiden University, Leiden, The Netherlands

Professor Rissmann explored the evolving landscape of topical therapies in psoriasis, emphasizing their continued relevance given that approximately 80% of patients have mild disease, and up to 50% regularly use topical treatments. While topical corticosteroids have been in use since the 1950s, the 1980s saw the introduction of vitamin D analogues and retinoids. More recent innovations include topical PDE4 inhibitors and aryl hydrocarbon receptor modulators.[1]

He outlined the key principles of topical drug delivery, focusing on three domains. The skin barrier function in psoriasis is impaired, partly due to altered ceramide composition in the stratum corneum, which can enhance drug penetration.[2] Drug properties, such as molecular size and physicochemical characteristics, influence absorption. The choice of vehicle, use of penetration enhancers, and keratolytic agents (e.g., salicylic acid) can significantly affect delivery efficiency.

Professor Rissmann further highlighted emerging innovations in topical therapies. Recent approvals include tapinarof, an aryl hydrocarbon receptor modulator that restores barrier function and reduces skin inflammation. Tapinarof was approved by the FDA in 2022 for plaque psoriasis. Roflumilast is an approved PDE4 inhibitor that increases intracellular cAMP, exerting broad anti-inflammatory effects. It is available in elegant formulations (e.g., cream, foam), which improve patient adherence. Currently, there are drug development studies ongoing on repurposed drugs in enhanced vehicles and microneedle-enabled delivery systems. Furthermore, there are novel topicals in development with novel targets, including the JAK pathway, senescence, immunometabolism, and skin microbiome modulation.

In summary, topical therapy remains a cornerstone of psoriasis management, and advances in formulation science and molecular targeting are opening new avenues for effective, patient-friendly treatments.

References:

1. 1. Psoriasis and Treatment: Past, Present, and Future Aspects. Reid C, Griffiths CEM. *Acta Derm Venereol*. 2020 Jan 30;100(3):adv00032.
2. Lesional Psoriasis is Associated with Alterations in the Stratum Corneum Ceramide Profile and Concomitant Decreases in Barrier Function. Rousel J, Mergen C, Bergmans ME, et al. *Exp Dermatol*. 2024 Oct;33(10):e15185.

Oral Drug Development: History and Future Prospects

Curdin Conrad, MD, IPC Councilor
Lausanne University Hospital, Lausanne, Switzerland

Professor Conrad provided a comprehensive overview of oral therapies' evolution and future direction in psoriasis, highlighting established treatments and emerging innovations.[1]

Currently, conventional oral agents such as methotrexate, dimethylfumarate, and acitretin remain first-line systemic options in many countries. These drugs offer a reasonable safety and efficacy profile and are more cost-effective than biologics. In contrast, biologics, including TNF, IL-17, and IL-23 inhibitors, are highly effective but incur higher costs.

In recent years, oral small molecules with novel mechanisms of action have been developed and approved, such as PDE4 inhibitors (e.g., apremilast) and TYK2 inhibitors (e.g., deucravacitinib). These oral agents offer improved safety and tolerability, though their efficacy remains somewhat lower than that of biologics.

Professor Conrad also discussed the next wave of oral therapies, including oral peptides targeting the IL-23 receptor, which have shown favorable efficacy and safety in clinical trials. Another example is oral TNF inhibitors, which are currently in development. However, several challenges lie ahead. Market crowding with multiple novel oral agents can lead to inter- and intra-class competition. There is also competition for the rise of generics (e.g., apremilast) and biosimilars (e.g., ustekinumab, secukinumab). Moreover, new oral therapies must compete with next-generation biologics with bimodal mechanisms and ultra-long-acting formulations, offering fewer injections and greater convenience.

Looking forward, Professor Conrad emphasized the importance of patient stratification based on clinical phenotype and molecular endotype. This approach could guide the selection of biologics or oral peptide therapeutics targeting specific cytokines and targeted synthetic disease-modifying drugs acting on broader immune pathways.[2]

Oral drug development in psoriasis is entering a new era of precision medicine, where clinical and molecular profiling will be key to personalized treatment selection and long-term disease control.

References:

1. Psoriasis and Treatment: Past, Present, and Future Aspects. Reid C, Griffiths CEM. *Acta Derm Venereol.* 2020 Jan 30;100(3):adv00032.
2. Immune Modules to Guide Diagnosis and Personalized Treatment of Inflammatory Skin Diseases. Seremet T, Di Domizio J, Girardin A, et al. *Nat Commun*. 2024 Dec 18;15(1):10688.

Transcriptomic Profiling of Hyperkeratotic Hand Eczema Skin with Comparison to Atopic Dermatitis and Psoriasis

Weixin Zhou, MD
University Medical Center Groningen, Groningen, The Netherlands

Dr. Zhou presented transcriptomic analyses aimed at characterizing hyperkeratotic hand eczema as a distinct clinical and molecular entity. Using bulk RNA sequencing, lesional (HL) and non-lesional (HN) palmar skin from patients with moderate to severe hyperkeratotic hand eczema were compared to healthy controls (HC). The analysis revealed 2,329 differentially expressed genes (DEGs) in HL versus HC, while HN skin showed only 318 DEGs, indicating a strong lesional-specific signature.

Upregulated genes in HL included markers of tissue-resident memory T cells (ZNF683), cytotoxic mediators (GZMB/K), and pro-inflammatory chemokines and cytokines (CXCL9/10, CCL18, IL-20/23A/26). These were enriched in pathways related to IFN-γ signaling, T-helper cell differentiation, and interleukin cascades. In contrast, downregulated genes were associated with lipid metabolism, epithelial barrier function, and structural integrity, including PLIN1/4, LEP, FLG2, and KRT19.

Gene set variation analysis revealed broad T-helper cell activation (Th1, Th2, Th17, Th22), enhanced IL-12/23 and IL-36 signaling, and strong TRM cell signatures in HL skin. Barrier-related pathways, including lipid synthesis and tight junctions, were notably impaired.

Hyperkeratotic hand eczema demonstrated a broader immune activation profile compared to public transcriptomic datasets of psoriasis and atopic dermatitis. While psoriasis was dominated by Th17/IL-36 and atopic dermatitis by Th2/JAK-STAT signatures, hyperkeratotic hand eczema showed overlapping features of both, with more pronounced TRM enrichment.

Hyperkeratotic hand eczema exhibits a unique transcriptomic profile that positions it between psoriasis and atopic dermatitis, with distinct immune and barrier dysfunction signatures. These findings support the classification of hyperkeratotic hand eczema as a separate immunopathological entity, which may have implications for targeted therapeutic strategies.

Predicting Probability of Psoriasis Biologic Drug Continuation: An Explainable Machine Learning Approach Applying Real-World Data

Amaani Hussain
Newcastle University, Newcastle upon Tyne, United Kingdom

Dr. Hussain presented a machine learning-based approach to predict biologic drug continuation in psoriasis patients, addressing the challenge that only one-third of patients in the UK remain on their initial biologic therapy due to loss of efficacy or adverse events.

Using real-world data from 10,806 biologic-naïve adult patients in the BADBIR registry (2007–2024), the study developed and validated predictive models for treatment persistence up to 36 months. The best-performing model was an XGBoost survival analysis, supported by random forest-based imputation for missing data. It achieved a C-index of 0.63 and Brier scores ≤0.23, indicating moderate predictive performance.

To ensure clinical interpretability, SHAP (Shapley Additive exPlanations) values were used to identify key predictors of drug continuation. The most influential variables included: i) initial biologic agent; ii) patient age; iii) recruitment center; iv) occupational status; v) baseline PASI score.

This explainable AI model offers a data-driven tool to support personalized treatment decisions in clinical practice. By identifying patients at risk of early discontinuation, clinicians may better tailor biologic choices, potentially improving long-term outcomes and reducing treatment failure.

This study demonstrates the potential of explainable machine learning models to enhance precision medicine in psoriasis care, leveraging real-world data to inform individualized therapeutic strategies.

Chronic Hand Eczema is a Type 2 Disease: Evidence from Integrated Clinical Trial and Molecular Profiling

Perrine Gery
Centre International de Recherche en Infectiologie (CIRI), Lyon, France

Dr. Gery presented integrated clinical and molecular data supporting the classification of chronic hand eczema as a type 2 immune-mediated disease. Chronic hand eczema is a heterogeneous and persistent inflammatory skin condition, often overlapping with atopic dermatitis, contact dermatitis, and psoriasis. The immunopathology of chronic hand eczema has remained poorly defined.

The study combined transcriptomic profiling within a phase 2b randomized, double-blind, placebo-controlled trial evaluating dupilumab in 94 adults with moderate to severe chronic hand eczema unresponsive to potent topical corticosteroids. Patients were treated over 16 weeks.

Molecular analyses revealed that type 2 immune responses were dominant across all chronic hand eczema subtypes, regardless of clinical presentation or etiology. Gene expression patterns showed similarities with both atopic dermatitis and psoriasis, involving dysregulation of: i) skin barrier function; ii) leukocyte migration; iii) cytotoxicity; and iv) mixed type 1, 2, and 3 immune pathways.

Treatment with dupilumab led to significant clinical and quality-of-life improvement in most patients. On a molecular level, dupilumab restored skin barrier gene expression and normalized immune signaling, highlighting IL-4Rα signaling as a central driver of chronic hand eczema pathogenesis.

This study provides compelling evidence that CHE is a type 2-driven disease, independent of environmental or atopic background. These findings support using IL-4/IL-13-targeted therapies, such as dupilumab, as promising treatment options for moderate to severe chronic hand eczema.

Psoriatic Fibroblasts Exhibit a Distinct Transcriptomic Profile

Lili Flink Borbala
University of Szeged, Szeged, Hungary

Dr. Borbala explored the role of dermal fibroblasts in the recurrence and persistence of psoriasis, focusing on their potential to retain inflammatory memory even after clinical resolution. While previous studies have shown that keratinocytes in resolved lesions maintain epigenetic changes, this study investigated whether fibroblasts from resolved psoriatic skin exhibit long-term molecular alterations.

Fibroblasts were isolated from healthy skin (H), non-lesional psoriatic skin (PS-NL), and resolved psoriatic skin of patients treated with systemic therapy. RNA sequencing revealed distinct transcriptional profiles across all groups.

Upregulated genes were associated with lipid metabolism in PS-NL vs. healthy skin, while downregulated genes involved stress response and gene regulation. In resolved psoriatic skin vs. healthy skin, increased expression was linked to MAPK1/3 activation and IL-6 signaling, whereas downregulated genes affected cell structure and division.

Direct comparison of PS-NL and resolved psoriasis skin fibroblasts revealed an upregulation of transcriptional regulators such as TP53, NOTCH4, and FOXO, and a downregulation of genes involved in ion transport, bicarbonate production, and syndecan signaling.

These findings suggest that fibroblasts from resolved psoriatic skin retain a distinct transcriptomic signature, indicative of inflammatory and proliferative memory. Moreover, fibroblasts from never-lesional psoriatic skin also showed subclinical alterations, implying a predisposition to lesion development even in clinically unaffected areas.

This study highlights the active role of dermal fibroblasts in psoriasis pathogenesis and recurrence. Both resolved and uninvolved skin harbor molecular imprints that may contribute to disease persistence, offering new insights into psoriatic memory beyond the epidermis.

Epithelial NF-κB Shapes the Innate and Adaptive Immune Landscape and Coordinates IL-17 Immunity

Divyaa Narayanan, BBiomed (Hons)
Frazer Institute, The University of Queensland, Brisbane, Australia

Dr. Narayanan presented mechanistic insights into how epithelial NF-κB signaling orchestrates innate and adaptive immune responses in psoriasis. While genome-wide association studies have implicated NF-κB-regulated genes in psoriasis susceptibility, the cell-type-specific role of NF-κB in skin inflammation remains incompletely understood.

A murine model was developed with epithelial-specific deletion of IκBα (IκBα$^{E\text{-}KO}$), which leads to constitutive NF-κB activation and causes the development of psoriasis-like skin lesions characterized by hyperkeratosis, immune cell infiltration, and elevated pro-inflammatory cytokines by postnatal day 7.

Multi-dimensional flow cytometry and qPCR analyses on IκBα$^{E\text{-}KO}$ mice revealed: i) expansion of macrophage and monocyte subsets, with differential MHC II and Ly6C expression; ii) increased IL-17a-producing γδ T cells; and iii) elevated IL-17a and IL-17f expression in lesional skin.

Neutralizing antibodies were administered postnatally to assess the functional role of IL-17 cytokines. IL-17a blockade prevented, and IL-17f inhibition ameliorated, the skin phenotype in IκBα$^{E\text{-}KO}$ mice. Further analysis confirmed distinct roles for IL-17a and IL-17f in regulating inflammation and immune cell composition.

This study demonstrates that epithelial NF-κB activation is sufficient to initiate IL-17-driven skin inflammation, highlighting its central role in eliciting γδ T cell responses and coordinating type 17 immunity. These findings underscore the importance of epithelial-immune crosstalk in psoriasis pathogenesis and suggest that targeting epithelial NF-κB or IL-17 pathways may offer therapeutic benefit.

IL-34 Expression and Function in Hidradenitis Suppurativa and Psoriasis

Emanuele Scala, PhD
Istituto Dermopatico dell'Immacolata, Rome, Italy

Dr. Scala presented new insights into the role of interleukin-34 (IL-34) in the pathogenesis of hidradenitis suppurativa (HS) and psoriasis. IL-34 is a keratinocyte-derived cytokine with immunoregulatory functions. While IL-34 has been increasingly studied in psoriasis, its involvement in HS has not been previously explored.

Transcriptomic analyses revealed that IL-34 is significantly downregulated in lesional skin of both HS and psoriasis compared to non-lesional areas. Single-cell RNA sequencing identified differentiated keratinocytes as the primary source of IL-34, with reduced expression in psoriatic lesions. Immunostaining confirmed this spatial pattern, showing IL-34 localization in the upper epidermis of healthy skin and its marked reduction in lesional areas.

In 2D and 3D epidermal models, IL-34 expression was suppressed by psoriasis-associated T-cell supernatants and anti-differentiative cytokines such as IL-22, suggesting that impaired keratinocyte maturation contributes to IL-34 downregulation.

Functionally, IL-34 activated ERK1/2 and STAT3 signaling in differentiated keratinocytes and regulated genes involved in tight junction formation and epidermal barrier integrity. Clinically, IL-34 expression was restored in psoriatic skin following treatment with anti-IL-17 or anti-IL-23 biologics, correlating with therapeutic response.

In conclusion, IL-34 is downregulated and mislocalized in both HS and psoriasis, which are Th17-driven inflammatory diseases. IL-34 restoration following Th17 pathway blockade suggests a role in re-establishing skin homeostasis and barrier function, thereby positioning IL-34 as a potential biomarker of disease activity and treatment response.

Rethinking Psoriasis Management: Targeting Disease Memory for Long-Term Modification

Georg Stary, MD
Medical University of Vienna, Vienna, Austria

Professor Stary discussed a paradigm shift in psoriasis management, focusing on targeting disease memory to achieve long-term disease modification. Psoriasis frequently relapses in previously affected skin regions, a phenomenon attributed to $CD8^+$tissue-resident memory T cells (TRM). Memory T cells persist in clinically resolved skin lesions and retain the capacity to produce IL-17 and IL-22. These TRMs are thus able to sustain and reignite skin inflammation.

The concept of disease modification was introduced as a holistic approach aimed at fundamentally altering the trajectory of psoriasis, rather than merely controlling symptoms. Central to this strategy is the early intervention hypothesis, which poses that early therapeutic targeting may prevent the establishment or persistence of pathogenic TRM cells.

Findings from the GUIDE study, a phase 3b, randomized, double-blinded trial, supported this hypothesis:[1]

- Superresponders to IL-23 inhibition showed a greater and more sustained decline in TRM cells compared to standard responders.
- Superresponders also exhibited higher levels of regulatory T cells (Tregs), suggesting a more favorable immune balance.
- However, regulatory TRM cells were found to be functionally impaired in psoriasis, potentially limiting their ability to counteract inflammation.
- IL-23 inhibition effectively targeted and reduced TRM populations, reinforcing its role in modifying disease memory and preventing relapse.

Professor Stary emphasized that targeting TRM cells, particularly by early IL-23 blockade, may offer a path toward durable remission in psoriasis. This approach redefines treatment success by aiming not only for symptom clearance but also for long-term immune reprogramming.

Reference:

1. Noninferiority of 16-Week vs 8-Week Guselkumab Dosing in Super Responders for Maintaining Control of Psoriasis: The GUIDE Randomized Clinical Trial. Eyerich K, Asadullah K, Pinter A, et al. *JAMA Dermatol*. 2024 Sep 1;160(9):953-963.

Early Intervention in Psoriasis: Guiding the Way to Disease Modification?

Enikö Sonkoly, MD, PhD
Karolinska Institutet, Stockholm, Sweden

Professor Sonkoly discussed the emerging concept of early intervention in psoriasis as a strategy to achieve disease modification. Disease modification is defined in a Delphi consensus study as a sustained improvement in the disease course of plaque psoriasis resulting from a change in pathophysiology that minimizes the need for treatment.[1] Disease modification can be evaluated by sustained BSA<1% / PGA 0/1 for >12 months following treatment cessation.

Patients with psoriasis duration under two years, especially those with ultrashort disease duration (<15 months), were significantly more likely to become superresponders to IL-23 inhibition, achieving complete skin clearance by week 28.[2] These patients also experienced longer disease-free intervals after treatment cessation. This suggests that early IL-23 inhibition may prevent the establishment of pathogenic tissue-resident memory T cells (TRMs) and promote an immune reset.

This data indicates that early biologic intervention, particularly IL-23 inhibitors, improves short-term efficacy and may delay relapse and extend remission after treatment discontinuation.

Professor Sonkoly advocated for a proactive treatment paradigm in psoriasis, where early, targeted therapy could lead to durable disease control and potentially modify the natural course of the disease.[3]

References:

1. An international Delphi consensus to define a clinically appropriate definition of disease modification for plaque psoriasis. Eyerich K, Krueger J, Stahle M, et al. *J Eur Acad Dermatol Venereol*. 2024 May;38(5):e424-e427.
2. Noninferiority of 16-Week vs 8-Week Guselkumab Dosing in Super Responders for Maintaining Control of Psoriasis: The GUIDE Randomized Clinical Trial. Eyerich K, Asadullah K, Pinter A, et al. *JAMA Dermatol*. 2024 Sep 1;160(9):953-963.
3. Long-term Outcomes and Prognosis in New-Onset Psoriasis. Svedbom A, Mallbris L, Larsson P, et al. *JAMA Dermatol*. 2021 Apr 14;157(6):1-8.

Oral Peptides in Psoriasis: The Next Frontier in Treatment Innovation

Diamant Thaci, MD, PhD, IPC Councilor
University of Lübeck, Lübeck, Germany

Professor Thaci gave an overview of novel oral peptides currently in development. One example is icotrokinra, a novel oral peptide therapy for psoriasis. Icotrokinra is a selective IL-23 receptor antagonist, composed of a short amino acid chain with a molecular weight of 1,898 Da. It is designed for oral administration, with no known off-treatment effects or drug interactions, offering a favorable safety and convenience profile.[1]

In the ICONIC-LEAD phase 3 clinical trial, icotrokinra demonstrated robust clinical efficacy:[2]

- IGA 0/1 response at week 24 in 74% of patients
- PASI 90 response in 64%
- Meaningful itch reduction in 73% of patients by week 24
- Icotrokinra showed notable improvements in scalp and genital psoriasis, areas often difficult to treat

The safety profile was comparable to placebo, and the drug demonstrated superiority over deucravacitinib, a TYK2 inhibitor, in terms of efficacy and tolerability.[2]

In summary, icotrokinra represents a new class of targeted oral therapies in psoriasis, combining biologic-like efficacy with the convenience of oral delivery. Its favorable safety, broad efficacy—including in special sites—and lack of drug interactions position it as a potential game-changer in the systemic treatment landscape of psoriasis.

References:

1. Translational Pharmacokinetics of Icotrokinra, a Targeted Oral Peptide that Selectively Blocks Interleukin-23 Receptor and Inhibits Signaling. Knight B, Tammara B, Modi NB, et al. *Dermatol Ther (Heidelb)*. 2025 Sep;15(9):2495-2520.
2. Once-daily oral icotrokinra versus placebo and once-daily oral deucravacitinib in participants with moderate-to-severe plaque psoriasis (ICONIC-ADVANCE 1 & 2): two phase 3, randomised, placebo-controlled and active-comparator-controlled trials. Gold LS, Armstrong AW, Bissonnette R, et al. *Lancet*. 2025 Sep 18:S0140-6736(25)01576-4.

Embracing the Known: Tracing the Evolution of Psoriasis

Lone Skov, MD, PhD, IPC Board Member
Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, Denmark

Professor Skov provided a historical overview of how our understanding of psoriasis has evolved from a keratinocyte-centric skin disorder to a systemic immune-mediated disease with complex comorbidities and psychosocial burden.[1]

She traced key milestones in psoriasis immunology:

- Pre-1980s: Psoriasis was viewed primarily as a disorder of keratinocyte hyperproliferation.
- 1980s: Introduction of the Th1/Th2 paradigm. Using the Nickoloff SCID mouse model, it was demonstrated that T cell transfer alone could induce psoriatic lesions, reframing psoriasis as a T cell–driven disease. This led to the recognition of cytokine signatures that define different psoriasis phenotypes.
- 1994: Identification of TNF-α as a central inflammatory mediator.
- 2000s onward: Refinement of the IL-23/IL-17 axis, now central to psoriasis pathogenesis.

Professor Skov emphasized that psoriasis is not a uniform disease. Instead, psoriasis encompasses diverse clinical subtypes, each potentially driven by distinct immune pathways. Th17 mainly drives plaque psoriasis. Erythrodermic psoriasis and paradoxical psoriasis reactions are driven by type 1 interferon. Pustular psoriasis is driven by neutrophilic inflammation.

This heterogeneity in immune pathways challenge the idea of a single immune driver and raises questions about therapy-recalcitrant psoriasis—specifically, what underlies biologic resistance in certain patients.[1]

In summary, Professor Skov advocated for a nuanced, phenotype-driven approach to psoriasis management, grounded in the evolving understanding of its immune complexity and systemic nature.[2]

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1. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. Armstrong AW, Read C. *JAMA*. 2020 May 19;323(19):1945-1960.
2. Multiple Biologics Treatment Failures in Patients with Psoriasis: A Case Series of 4 Patients. Jensen MB, Loft N, Zachariae C, et al. *Acta Derm Venereol*. 2025 Mar 9;105:adv42987.

Illuminating the Layers: Uncovering Immune Sophistication in Psoriasis

Curdin Conrad, MD, IPC Councilor
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Professor Conrad explored the complex immune architecture of psoriasis, challenging the oversimplified view of the disease as solely IL-23/IL-17-driven. He emphasized that psoriasis involves distinct immune phases and multiple overlapping cytokine pathways, requiring a more nuanced understanding of psoriasis pathogenesis.

In the early phase of disease development, type I interferon responses dominate, while the late phase of psoriasis is characterized by Th17-driven inflammation. This temporal evolution suggests that psoriasis is not static but exists along a dynamic immunological continuum.

Through transcriptomic and immunological profiling, three immune endotypes were identified:[1]

i) Th17 endotype: associated with plaque psoriasis
ii) Neutrophilic endotype: linked to pustular forms
iii) Type I interferon endotype: observed in paradoxical and erythrodermic psoriasis

Importantly, non-pustular psoriasis was shown to lie along a type I interferon–Th17 continuum, rather than fitting into discrete categories. This immune heterogeneity challenges phenotype-based assumptions and underscores the need for precision immunotyping in clinical practice.

Professor Conrad also discussed therapeutic implications, highlighting the potential of multispecific targeting strategies. PDE4 inhibitors can be applied for their broad anti-inflammatory effects. This is also the case for TYK2 inhibitors, which modulate IL-23, type I IFN, and IL-12 signaling with greater selectivity than broader JAK inhibitors, potentially reducing off-target effects. He also noted that UV therapy depletes plasmacytoid dendritic cells (pDCs), a particularly effective mechanism in guttate psoriasis. Furthermore, cyclosporin remains a valuable option in acute, unstable disease.

In summary, Professor Conrad advocated for reimagining psoriasis pathogenesis—from a single-pathway model to a layered, dynamic immune network—to better inform targeted and phase-specific interventions.

Reference:

1. Immune Modules to Guide Diagnosis and Personalized Treatment of Inflammatory Skin Diseases. Seremet T, Di Domizio J, Girardin A, et al. *Nat Commun.* 2024 Dec 18;15(1):10688.

RNA-Based Modulation and Targeting of Skin Inflammation in Psoriasis and Atopic Dermatitis

Ana Rebane, PhD
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Professor Rebane presented cutting-edge research on RNA-based strategies to modulate skin inflammation in psoriasis and atopic dermatitis (AD). RNA molecules have the potential to serve as both biomarkers and therapeutic agents.

Non-coding RNAs, including microRNAs and long non-coding RNAs (lncRNAs), regulate immune responses, keratinocyte function, and barrier integrity in psoriasis and other inflammatory skin diseases. These RNA species influence key signaling pathways such as NF-κB, JAK/STAT, and IL-17/IL-23, which are central to psoriasis and atopic dermatitis pathogenesis.[2]

Professor Rebane also discussed the development of RNA-targeted therapies, including:

- Antisense oligonucleotides (ASOs) to silence pro-inflammatory genes
- Small interfering RNAs (siRNAs) to block cytokine signaling
- RNA mimics to restore regulatory functions

These approaches offer high specificity, tunable effects, and the potential for topical or localized delivery, minimizing systemic side effects.

In preclinical models, RNA-based interventions successfully modulated inflammatory gene expression, reduced cytokine production, and improved epidermal barrier function. Moreover, RNA signatures may serve as diagnostic tools to stratify patients and predict treatment response.

In summary, Professor Rebane highlighted RNA-based modulation as a promising novel approach in treating chronic inflammatory skin diseases, offering precision targeting of immune pathways and the potential for personalized, disease-modifying therapies.

References:

1. MiRNA Expression Profiles of the Perilesional Skin of Atopic Dermatitis and Psoriasis Patients are Highly Similar. Carreras-Badosa G, Maslovskaja J, Vaher H, et al. *Sci Rep*. 2022 Dec 31;12(1):22645.
2. MiR-146b Probably Assists miRNA-146a in the Suppression of Keratinocyte Proliferation and Inflammatory Responses in Psoriasis. Hermann H, Runnel T, Aab A, et al. *J Invest Dermatol*. 2017 Sep;137(9):1945-1954.

Extracellular NAMPT Promotes Keratinocyte Hyperproliferation and Inflammation via TLR4/TLR2 Pathways and Contributes to Psoriasis Symptoms in an Imiquimod-Induced Mouse Model

Luca Sanna, PhD
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Luca Sanna presented novel insights into the role of extracellular NAMPT (eNAMPT) as a pro-inflammatory mediator in psoriasis. While NAMPT is traditionally known for its intracellular metabolic functions, this study focused on its extracellular cytokine-like activity, particularly in keratinocyte biology and immune activation.

eNAMPT expression is upregulated by TNF-α and IFN-γ, and it acts paracrinally on endothelial cells, enhancing leukocyte recruitment. In keratinocytes, eNAMPT promotes hyperproliferation by activating molecular pathways typically suppressed in differentiated cells. eNAMPT also amplifies IL-22-driven inflammation via TLR2 signaling. In an imiquimod-induced mouse model of psoriasis, administration of eNAMPT worsened clinical symptoms, including erythema, scaling, and PASI scores. Conversely, treatment with an eNAMPT-neutralizing antibody significantly improved disease severity. Mechanistically, blocking eNAMPT interrupts IL-23/IL-17 axis activation, reduces keratinocyte stress responses, enhances terminal differentiation, and restores epidermal homeostasis

In summary, eNAMPT mimics IL-22-like effects in keratinocytes, driving both proliferation and inflammatory cytokine production. These findings position extracellular NAMPT as a novel therapeutic target in psoriasis, potentially modulating both immune signaling and epidermal dysfunction.

Psoriasis and Epidermal Innervation

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Coming Soon.

From Rare to Frequent: How Immunogenetics Enlightens the Role of the Type I IFN Pathway in Psoriasis

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Coming Soon.