



MAY 2025

A Report from the 2025 Society for Investigative Dermatology (SID) Annual Meeting

Rundong Jiao

+

Huidi Shucheng, MD, PhD, MPH, 2024 IPC Fellow

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS

INTRODUCTION

The 2025 Society of Investigative Dermatology (SID) Annual Meeting took place in San Diego, California, United States, from Wednesday, May 7, to Saturday, May 10, 2025. Over 1,200 basic and clinical scientists interested in dermatology attended the event. With more than 50 congress sessions and over 300 presentations, the meeting was filled with a diverse community of scientists who came to exchange information on the latest advances. This report provides an overview of the key psoriasis sessions, including the IPC Symposium: Not the Usual Suspects – Lesser Known Cells in Psoriasis.

TABLE OF CONTENTS

IPC Symposium: Not the Usual Suspects – Lesser Known Cells in Psoriasis

Summaries written by: Rundong Jiang

4 **Overview of Psoriasis Pathogenesis**
Johann Gudjonsson, MD, PhD, IPC Board Member

6 **Neutrophils and Psoriasis**
Francesca Capon, PhD, IPC Councilor

8 **Fibroblasts and Psoriasis**
Satveer Mahil, PhD, FRCP, IPC Councilor

9 **Melanocytes and Psoriasis**
Mehdi Rashighi, MD

11 **Endothelial Cells and Psoriasis**
Michael Garshick, MD, IPC Councilor

12 **Nerve Cells and Psoriasis**
Daniel Kaplan, MD, PhD

Abstract Presentations

Abstract summaries provided by original presenters and published with their permission.

13 **Regulation of IL-6 and Calcitonin Gene-related Peptide (CGRP) Expression by Vitamin (VD) in Transformed Dorsal Root Ganglion (DRG) Cells**
Richard D. Granstein, MD

14 **Neutrophils are Primed for Enhanced Inflammasome Activation in Skin Microvasculature During Adhesion via E-selectin**
Yoshiaki Matsushima, MD, PhD

TABLE OF CONTENTS (continued)

Other Psoriasis Sessions

Summaries written by: Huidi Shucheng, MD, PhD, MPH, 2024 IPC Fellow

- | | |
|-----------|--|
| 15 | A Senescent Subpopulation of Fibroblasts Induce Inflammation in Psoriasis through APOE
Qiaochu Jiang, MD |
| 16 | Eugene Farber Lecture – Psoriasis: From Molecular Endotypes to Treatment Resistance
Michel Gilliet, MD, IPC Councilor |
| 17 | IL-17 Inhibitors vs. Methotrexate in Preventing New-Onset Psoriatic Arthritis in Psoriasis Patients: A Retrospective Population-Level Analysis
Ryan Chan, MD |
| 18 | IL-17D-Induced Metabolic Reprogramming Empowers Inflammatory Memory in Keratinocytes to Promote Psoriasis Relapse
Yuping Lai, PhD |
| 19 | AX-158 Proof-of-Mechanism Safety Study: Evaluating a Novel T Cell Receptor (TCR) Signal Modulator in Patients with Mild-to-Moderate Plaque Psoriasis
Christopher VanDeusen, PhD |
| 20 | Efficacy and Safety of Once-Daily Roflumilast Foam 0.3% for Psoriasis of the Scalp and Body Involving Knees/Elbows: Subgroup Results from the Phase 3 Arrector Trial
Saori Kato, PhD |
| 21 | Unveiling the IL-36/IFNκ Axis in Sex-Biased Generalized Pustular Psoriasis
Mrinal Sarkar, PhD |

Overview of Psoriasis Pathogenesis

Johann Gudjonsson, MD, PhD, IPC Board Member

University of Michigan, Department of Dermatology, Ann Arbor, Michigan, United States

Psoriasis is a chronic, immune-mediated skin disease affecting over 60 million people worldwide¹. It typically presents in adolescence or early adulthood and persists lifelong, with no gender predilection. Up to 25% of patients develop psoriatic arthritis¹. Beyond physical manifestations, psoriasis profoundly impacts psychosocial well-being, contributing to lower self-esteem, social rejection, depression, and increased risk of suicidal ideation.

Histologically, psoriasis is characterized by hyperproliferation of keratinocytes, perivascular lymphocytic and dendritic cell infiltrates, and regenerative epithelial maturation akin to wound healing². Clinically, it encompasses diverse subtypes, including plaque, inverse, erythrodermic, and pustular variants, underpinned by distinct immune signatures, including T-cell-driven IL-17A responses and neutrophil-dominant IL-36 pathways³.

Genetically, psoriasis susceptibility involves over 160 loci affecting pathways such as IL-23/Th17 signaling, epidermal differentiation, interferon responses, and TNF/NF- κ B activation⁴. Recently, several studies identified that, in addition to classical immune pathways, the pathogenesis of psoriasis involves a broad range of non-immune cell types. Traditionally overlooked melanocytes contribute to local immune modulation and may activate CD8⁺ Tc17 cells⁵. Nerve injury has been associated with spontaneous resolution of psoriatic lesions, suggesting an important role for neuroimmune interactions⁶. Endothelial cells facilitate leukocyte trafficking and maintain an activated vascular state that perpetuates inflammation⁷. Fibroblasts, similarly, remodel the extracellular matrix and secrete pro-inflammatory mediators, reinforcing psoriasis chronicity⁸. Neutrophils act as major amplifiers of inflammation through the release of cathepsin G, elastase, and protease 3, further activating IL-36 signaling⁹. These findings depict psoriasis as a multicellular, cytokine-driven disease extending beyond adaptive immunity, highlighting complex interactions between immune and structural cells.

References:

1. Parisi R, Iskandar IYK, Kontopantelis E, et al. National, Regional, and Worldwide Epidemiology of Psoriasis: Systematic Analysis and Modelling Study. *BMJ*. 2020;369:m1590. Published 2020 May 28. doi:10.1136/bmj.m1590
2. Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of Psoriasis. *Annu Rev Immunol*. 2014;32:227-255. doi:10.1146/annurev-immunol-032713-120225
3. Griffiths CEM, Armstrong AW, Gudjonsson JE, et al. Psoriasis. *Lancet*. 2021;397(10281):1301-1315. doi:10.1016/S0140-6736(20)32549-6
4. Dand N, Stuart PE, Bowes J, et al. GWAS Meta-Analysis of Psoriasis Identifies New Susceptibility Alleles Impacting Disease Mechanisms and Therapeutic Targets. *Nat Commun*. 2025;16(1):2051. doi:10.1038/s41467-025-56719-8

5. Prinz JC. Melanocytes: Target Cells of an HLA-C*06:02-Restricted Autoimmune Response in Psoriasis. *J Invest Dermatol.* 2017;137(10):2053-2058. doi:10.1016/j.jid.2017.05.023
6. Wang TS, Tsai TF. Psoriasis Sparing the Lower Limb with Postpoliomyelitis Residual Paralysis. *Br J Dermatol.* 2014;171(2):429-431. doi:10.1111/bjd.12854
7. Li Q, Shao S, Zhu Z, et al. An IGFBP7hi Endothelial Cell Subset Drives T Cell Extravasation in Psoriasis via Endothelial Glycocalyx Degradation. *J Clin Invest.* 2023;133(9):e160451. doi:10.1172/JCI160451
8. Ma F, Plazyo O, Billi AC, et al. Single Cell and Spatial Sequencing Define Processes by Which Keratinocytes and Fibroblasts Amplify Inflammatory Responses in Psoriasis. *Nat Commun.* 2023;14(1):3455. doi:10.1038/s41467-023-39020-4
9. Marrakchi S, Puig L. Pathophysiology of Generalized Pustular Psoriasis. *Am J Clin Dermatol.* 2022;23(Suppl 1):13-19. doi:10.1007/s40257-021-00655-y

Neutrophils and Psoriasis

Francesca Capon, PhD, IPC Councilor

University of British Columbia, Vancouver, Canada

Neutrophils, the most abundant circulating leukocytes, are increasingly recognized as key contributors to psoriasis pathogenesis. Neutrophil infiltration is a histological hallmark of psoriatic lesions, with elevated neutrophil-to-leukocyte ratios correlating with disease activity and therapeutic response¹. In generalized pustular psoriasis (GPP), recessive IL36RN mutations result in overactivated IL-36 signaling, promoting neutrophil accumulation and activation through enhanced inflammatory chemokine production². Although human neutrophils lack IL-36 receptors, neutrophil-derived proteases activate IL-36 cytokines, creating a feed-forward inflammatory loop with keratinocytes in skin lesions³. Additionally, mutations in the MPO gene lead to dysfunctional myeloperoxidase activity, impair neutrophil apoptosis, and result in elevated neutrophil counts and sustained inflammation⁴.

In plaque psoriasis, neutrophil infiltration progresses from the dermis to the epidermis, accompanied by upregulation of IL-8 and CD66 expression and enhanced migratory capacity⁵. Neutrophil activity is further amplified by IL-17 and IL-19 signaling, which promote chemokine expression, while MMP-9 enhances vascular permeability and T-cell infiltration⁶. A critical pathogenic feature involves the formation of neutrophil extracellular traps (NETs)—web-like DNA-protein structures expelled during a specialized form of neutrophil death known as NETosis⁷. NETs, initially intended for pathogen defense, propagate inflammation by activating keratinocytes, dendritic cells, and Th17 cells⁸. In psoriasis, NET formation is markedly increased, with contributions from low-density granulocytes and pro-inflammatory CXCR4+ neutrophil subsets⁹. While advances in spatial transcriptomics and genetic studies are expected to further elucidate neutrophil-mediated mechanisms, present findings highlight neutrophils as central amplifiers of inflammation and key drivers of disease progression in both pustular and plaque psoriasis.

References:

1. Näslund-Koch C, Kvist-Hansen A, Bojesen SE, et al. Low-Grade Systemic Inflammation is Associated with Risk of Psoriasis in a General Population Study of More Than 100,000 Individuals. *Br J Dermatol*. Published online April 18, 2025. doi:10.1093/bjd/ljaf147
2. Hussain S, Berki DM, Choon SE, et al. IL36RN Mutations Define a Severe Autoinflammatory Phenotype of Generalized Pustular Psoriasis. *J Allergy Clin Immunol*. 2015;135(4):1067-1070.e9. doi:10.1016/j.jaci.2014.09.043
3. Yuan ZC, Xu WD, Liu XY, et al. Biology of IL-36 Signaling and Its Role in Systemic Inflammatory Diseases. *Front Immunol*. 2019;10:2532. Published 2019 October 31. doi:10.3389/fimmu.2019.02532
4. Vergnano M, Mockenhaupt M, Benzian-Olsson N, et al. Loss-of-Function Myeloperoxidase Mutations Are Associated with Increased Neutrophil Counts and Pustular Skin Disease [published correction appears in *Am J Hum Genet*. 2021 Apr 1;108(4):757. doi: 10.1016/j.ajhg.2021.03.001.]. *Am J Hum Genet*. 2020;107(3):539-543. doi:10.1016/j.ajhg.2020.06.020

5. Albanesi C, Scarponi C, Pallotta S, et al. Chemerin Expression Marks Early Psoriatic Skin Lesions and Correlates with Plasmacytoid Dendritic Cell Recruitment. *J Exp Med*. 2009;206(1):249-258. doi:10.1084/jem.20080129
6. Sieminska I, Pieniawska M, Grzywa TM. The Immunology of Psoriasis-Current Concepts in Pathogenesis. *Clin Rev Allergy Immunol*. 2024;66(2):164-191. doi:10.1007/s12016-024-08991-7
7. Shao S, Fang H, Dang E, et al. Neutrophil Extracellular Traps Promote Inflammatory Responses in Psoriasis via Activating Epidermal TLR4/IL-36R Crosstalk. *Front Immunol*. 2019;10:746. Published 2019 April 5. doi:10.3389/fimmu.2019.00746
8. Lambert S, Hambro CA, Johnston A, et al. Neutrophil Extracellular Traps Induce Human Th17 Cells: Effect of Psoriasis-Associated TRAF3IP2 Genotype. *J Invest Dermatol*. 2019;139(6):1245-1253. doi:10.1016/j.jid.2018.11.021
9. Chen J, Bai Y, Xue K, et al. CREB1-driven CXCR4^{hi} Neutrophils Promote Skin Inflammation in Mouse Models and Human Patients. *Nat Commun*. 2023;14(1):5894. Published 2023 September 22. doi:10.1038/s41467-023-41484-3

Fibroblasts and Psoriasis

Satveer Mahil, PhD, FRCP, IPC Councilor

St. John's Institute of Dermatology, London, United Kingdom

Fibroblasts, the principal mesenchymal cells of the dermis, are essential for maintaining skin architecture through extracellular matrix synthesis, immune regulation, and mechanical support¹. Single-cell RNA sequencing analyses have delineated diverse fibroblast subsets in healthy skin, each occupying discrete spatial and functional niches. This cellular heterogeneity endows fibroblasts with the capacity to adapt dynamically to physiological and pathological stimuli. In inflammatory diseases like psoriasis, fibroblasts leverage this plasticity to adopt disease-associated states, fueling chronic inflammation and maladaptive tissue remodeling.

Recently, Dr. Mahil conducted single-cell RNA sequencing profiling of psoriatic lesions during early resolution following IL-23 blockade, providing critical insights into fibroblast dynamics². This analysis identified a specific expansion of pro-inflammatory fibroblast populations within psoriasis lesions, notably myofibroblast-like cells expressing high levels of WNT5A, IL-24, and CXCL8. Functional studies revealed that the formation of these inflammatory fibroblasts is strongly induced by IL-17A and TNF signaling, which synergistically upregulate pro-inflammatory gene programs within fibroblasts. These activated fibroblasts, predominantly localized to the upper dermis, contribute to disease maintenance by promoting keratinocyte proliferation, enhancing leukocyte infiltration, and sustaining chronic inflammation. Importantly, therapeutic inhibition of the IL-23 pathway led to rapid transcriptional reprogramming of fibroblasts, with attenuation of the pro-inflammatory signatures, highlighting the dynamic and reversible nature of fibroblast activation in psoriasis.

Collectively, recent studies establish fibroblasts not merely as passive structural components but as active orchestrators of psoriasis pathogenesis. Inflammatory fibroblasts modulate the immune microenvironment by recruiting T cells, neutrophils, macrophages, and dendritic cells into the skin. Fibroblast-derived mediators such as PGE2 and TNC further enhance neuroimmune interactions and sustain IL-23-driven inflammation³. Through these dual effects on epidermal and immune compartments, fibroblasts critically shape psoriatic inflammation's initiation, amplification, and persistence.

References:

1. Plikus MV, Wang X, Sinha S, et al. Fibroblasts: Origins, Definitions, and Functions in Health and Disease. *Cell*. 2021;184(15):3852-3872. doi:10.1016/j.cell.2021.06.024
2. Francis L, McCluskey D, Ganier C, et al. Single-Cell Analysis of Psoriasis Resolution Demonstrates an Inflammatory Fibroblast State Targeted by IL-23 Blockade. *Nat Commun*. 2024;15(1):913. doi:10.1038/s41467-024-44994-w
3. Chen X, Wu Y, Jia S, et al. Fibroblast: A Novel Target for Autoimmune and Inflammatory Skin Diseases Therapeutics. *Clin Rev Allergy Immunol*. 2024;66(3):274-293. doi:10.1007/s12016-024-08997-1

Melanocytes and Psoriasis: Culprit, Bystander, or Amplifier?

Mehdi Rashighi, MD

University of Massachusetts Medical School, Worcester, Massachusetts, United States

The potential involvement of melanocytes in psoriasis pathogenesis has garnered increasing interest¹. Drawing lessons from vitiligo, where melanocyte-specific CD8⁺ T cells and autoantigens such as MART-1 and tyrosinase are well-characterized, some hypotheses propose a similar autoimmune targeting of melanocytes in psoriasis². Clinical observations, including the Woronoff ring phenomenon, suggest melanocyte dysfunction during psoriatic inflammation³. Additionally, cytokines central to psoriasis, notably IL-17 and TNF, have been shown to synergistically suppress melanogenesis, potentially contributing to pigmentary alterations seen in lesions⁴.

Despite these observations, genetic studies firmly establish that psoriasis is primarily an immune-driven disease, with genome-wide association studies (GWAS) highlighting immune pathways rather than melanocyte-specific genes⁵. Nevertheless, emerging evidence indicates that melanocytes are not entirely passive. In psoriatic skin, melanocytes can express the psoriasis-associated autoantigen ADAMTSL5, particularly in HLA-C*06:02 positive individuals⁶. Furthermore, spatial transcriptomic analyses reveal intriguing colocalization of Tc17 cells and melanocytes within psoriatic lesions, suggesting melanocytes may amplify immune activation locally by presenting autoantigens to pathogenic T cells.

Genetic risk factors, particularly variants in HLA-C*06:02 and ERAP1, are pivotal in initiating psoriatic autoimmunity by altering antigen processing and presentation pathways⁷. HLA-C*06:02 encodes an MHC class I molecule that presents endogenous peptides to CD8⁺ T cells, while ERAP1 is involved in trimming peptides within the endoplasmic reticulum for optimal MHC-I loading. In psoriasis, dysregulated ERAP1 activity may generate aberrant melanocyte-derived peptides presented by HLA-C*06:02 molecules on melanocytes. This aberrant antigen presentation primes autoreactive CD8⁺ T cells, leading to their activation within the epidermis⁸.

Dr. Rashighi emphasized that CD8⁺ T cells differentiate into Tc17 cells under the influence of IL-23 signaling and that Tc17 cells produce pro-inflammatory cytokines, including IL-17A, IL-22, and IFN- γ , which sustain keratinocyte hyperproliferation and amplify local inflammation⁹.

References:

1. Arakawa A, Siewert K, Stöhr J, et al. Melanocyte Antigen Triggers Autoimmunity in Human Psoriasis. *J Exp Med*. 2015;212(13):2203-2212. doi:10.1084/jem.20151093
2. Brajac I, Kastelan M, Prpić-Massari L, et al. Melanocyte as a Possible Key Cell in the Pathogenesis of Psoriasis Vulgaris. *Med Hypotheses*. 2009;73(2):254-256. doi:10.1016/j.mehy.2009.01.048
3. Prinz JC. The Woronoff Ring in Psoriasis and the Mechanisms of Postinflammatory Hypopigmentation. *Acta Derm Venereol*. 2020;100(3):adv00031. doi:10.2340/00015555-3385

4. Wang CQF, Akalu YT, Suarez-Farinas M, et al. IL-17 and TNF Synergistically Modulate Cytokine Expression While Suppressing Melanogenesis: Potential Relevance to Psoriasis. *J Invest Dermatol.* 2013;133(12):2741-2752. doi:10.1038/jid.2013.237
5. Dand N, Stuart PE, Bowes J, et al. GWAS Meta-Analysis of Psoriasis Identifies New Susceptibility Alleles Impacting Disease Mechanisms and Therapeutic Targets. *Nat Commun.* 2025;16(1):2051. doi:10.1038/s41467-025-56719-8
6. Arakawa A, Siewert K, Stöhr J, et al. Melanocyte Antigen Triggers Autoimmunity in Human Psoriasis. *J Exp Med.* 2015;212(13):2203-2212. doi:10.1084/jem.20151093
7. Genetic Analysis of Psoriasis Consortium & the Wellcome Trust Case Control Consortium 2, Strange A, Capon F, et al. A Genome-Wide Association Study Identifies New Psoriasis Susceptibility Loci and an Interaction Between HLA-C and ERAP1. *Nat Genet.* 2010;42(11):985-990. doi:10.1038/ng.694
8. Arakawa A, Reeves E, Vollmer S, et al. ERAP1 Controls the Autoimmune Response against Melanocytes in Psoriasis by Generating the Melanocyte Autoantigen and Regulating Its Amount for HLA-C*06:02 Presentation. *J Immunol.* 2021;207(9):2235-2244. doi:10.4049/jimmunol.2100686
9. Prinz JC. Melanocytes: Target Cells of an HLA-C*06:02-Restricted Autoimmune Response in Psoriasis. *J Invest Dermatol.* 2017;137(10):2053-2058. doi:10.1016/j.jid.2017.05.023

Vascular Endothelial Cell Damage in Psoriasis: Mechanisms and Therapeutic Strategies

Michael Garshick, MD, MS, Assistant Professor of Medicine and Dermatology, IPC Councilor
New York University Langone Health, New York, New York, United States

Traditionally viewed as a cutaneous disease, psoriasis is increasingly recognized as a systemic inflammatory disorder with significant cardiovascular implications. Epidemiological studies show that patients with psoriasis, particularly those with severe disease, have a markedly elevated risk of myocardial infarction, independent of traditional cardiovascular risk factors¹. Beyond dyslipidemia and hypertension, psoriasis promotes vascular injury through persistent immune activation, with endothelial damage emerging as a critical early event in atherogenesis². Mechanistic studies demonstrate that inflammatory mediator of psoriatic skin, including IL-17A, TNF- α , and IL-6, contributes to endothelial activation and dysfunction³.

Dr. Garshick and his colleagues previously conducted transcriptomic analyses on endothelial cells, revealing upregulation of inflammatory pathways in both the skin and vascular endothelium, with evidence of NF- κ B pathway activation in psoriatic lesions³. Moreover, platelet hyperactivation, aggregation, and adhesion to endothelial cells are prominent features in psoriasis, further exacerbating vascular inflammation⁴. Another RNA sequencing study by Dr. Garshick's team identified a distinct platelet transcriptomic signature in psoriasis, characterized by upregulation of pathways related to fibrin clotting and platelet activation. This aberrant platelet gene expression profile correlated with vascular dysfunction, underscoring the systemic impact of platelet-endothelial interactions in psoriatic patients.

Therapeutically, biologic agents targeting IL-17 and TNF pathways have shown promise in reducing vascular inflammation and improving cardiovascular profiles. Adjunctive strategies, including low-dose aspirin and statin therapy, also demonstrate efficacy in attenuating endothelial activation^{4,5}. These findings emphasize the need for integrated cardiovascular risk management in psoriasis care, highlighting vascular inflammation as both a mechanistic link and a therapeutic target in mitigating cardiovascular disease burden in this patient population.

References:

1. Gelfand JM, Neimann AL, Shin DB, et al. Risk of Myocardial Infarction in Patients with Psoriasis. *JAMA*. 2006;296(14):1735-1741. doi:10.1001/jama.296.14.1735
2. Björkegren JLM, Lusis AJ. Atherosclerosis: Recent Developments. *Cell*. 2022;185(10):1630-1645. doi:10.1016/j.cell.2022.04.004
3. Garshick MS, Barrett TJ, Wechter T, et al. Inflammasome Signaling and Impaired Vascular Health in Psoriasis. *Arterioscler Thromb Vasc Biol*. 2019;39(4):787-798. doi:10.1161/ATVBAHA.118.312246
4. Garshick MS, Tawil M, Barrett TJ, et al. Activated Platelets Induce Endothelial Cell Inflammatory Response in Psoriasis via COX-1. *Arterioscler Thromb Vasc Biol*. 2020;40(5):1340-1351. doi:10.1161/ATVBAHA.119.314008
5. Garshick MS, Drenkova K, Barrett TJ, et al. A Randomized Open-Label Clinical Trial of Lipid-Lowering Therapy in Psoriasis to Reduce Vascular Endothelial Inflammation. *J Invest Dermatol*. 2022;142(6):1749-1752.e4. doi:10.1016/j.jid.2021.07.190

Nerve Cells and Psoriasis

Daniel H. Kaplan, MD, PhD

University of Pittsburgh, Pittsburgh, Pennsylvania, United States

Peripheral nociceptors, particularly those expressing TRPV1, are increasingly recognized as sensors of environmental stimuli and active participants in cutaneous immune regulation¹. Dr. Kaplan and other researchers demonstrated that TRPV1⁺ neurons are necessary for multiple skin inflammation models, including responses to *Candida albicans*², house dust mite allergens³, and irritant contact dermatitis⁴.

Pathogens and inflammatory mediators can directly activate these neurons, triggering local immune responses independent of tissue damage⁵. Through optogenetic activation, their team showed that stimulation of TRPV1⁺ nociceptors alone can induce robust Type 17 inflammation characterized by upregulation of IL-23, IL-6, IL-17, and IL-22⁵. Interestingly, sustained IL-23 expression requires repeated neuronal activation, indicating that temporal stimulation patterns shape immune outcomes. Moreover, TRPV1 activation leads to substance P-mediated mast cell degranulation, critical for initiating dermal dendritic cell clustering and subsequent IL-23 production. Intriguingly, Mrgprb2-deficient mice fail to mount appropriate inflammatory responses following neuronal stimulation, underscoring that effective neuro-immune cross-talk in the skin depends on direct communication between TRPV1⁺ nociceptors and mast cells.

In summary, this neuroimmune circuit culminates in anticipatory innate immunity, wherein TRPV1⁺ neurons, mast cells, and dermal dendritic cells collaborate to rapidly trigger IL-17-mediated host defense responses upon secondary pathogen encounter. These findings redefine nociceptors as integral components of skin immune surveillance, providing critical insights into the pathophysiology of inflammatory skin diseases and offering novel therapeutic targets within the neuroimmune axis.

References:

1. Kashem SW, Riedl MS, Yao C, et al. Nociceptive Sensory Fibers Drive Interleukin-23 Production from CD301b+ Dermal Dendritic Cells and Drive Protective Cutaneous Immunity. *Immunity*. 2015;43(3):515-526. doi:10.1016/j.immuni.2015.08.016
2. Kashem SW, Igyarto BZ, Gerami-Nejad M, et al. *Candida Albicans* Morphology and Dendritic Cell Subsets Determine T Helper Cell Differentiation. *Immunity*. 2015;42(2):356-366. doi:10.1016/j.immuni.2015.01.008
3. Serhan N, Basso L, Sibilano R, et al. House Dust Mites Activate Nociceptor-Mast Cell Clusters to Drive Type 2 Skin Inflammation. *Nat Immunol*. 2019;20(11):1435-1443. doi:10.1038/s41590-019-0493-z
4. Zhang S, Edwards TN, Chaudhri VK, et al. Nonpeptidergic Neurons Suppress Mast Cells via Glutamate to Maintain Skin Homeostasis. *Cell*. 2021;184(8):2151-2166.e16. doi:10.1016/j.cell.2021.03.002
5. Cohen JA, Edwards TN, Liu AW, et al. Cutaneous TRPV1⁺ Neurons Trigger Protective Innate Type 17 Anticipatory Immunity. *Cell*. 2019;178(4):919-932.e14. doi:10.1016/j.cell.2019.06.022

Regulation of IL-6 and Calcitonin Gene-related Peptide (CGRP) Expression by Vitamin (VD) in Transformed Dorsal Root Ganglion (DRG) Cells

Richard D. Granstein, MD

Department of Dermatology, Weill Cornell Medicine, New York, New York, United States

Introduction

Th17 helper T cells and IL-17 are generally accepted as playing essential roles in the pathogenesis of psoriasis. IL-6 contributes to the generation and maintenance of Th17 cells, while CGRP can also favor the differentiation of Th17 cells through defined pathways. Some evidence suggests that CGRP itself may play a role in psoriasis. Additionally, sensory nerves are implicated in psoriasis and Th17-type inflammation; for instance, denervation of psoriatic skin improves the condition, and proper innervation is necessary for full psoriasiform expression in animal models. Sensory neurons are known to produce IL-6 and CGRP, suggesting they may contribute to disease pathology.

Method

To explore whether agents that improve psoriasis inhibit the production of IL-6 and CGRP by sensory neurons, the researchers conducted preliminary experiments using vitamin D. Murine transformed DRG neurons (MED17.11 cells), which express markers of sensory neuron progenitors, were used as a surrogate for primary DRG neurons. These cells were cultured in differentiation medium containing fibroblast growth factor 2, dibutyryl cAMP, forskolin, nerve growth factor, Y-27632, and glial cell-derived neurotrophic factor, leading them to express markers of mature DRG neurons. The cells were then treated with 25-hydroxyvitamin D3 [25(OH)D3] and 1,25-dihydroxyvitamin D3 [1,25(OH)2D3].

Results

Both forms of vitamin D—25(OH)D3 and 1,25(OH)2D3—significantly inhibited IL-6 content in supernatants and CGRP content in lysates in a dose-dependent manner. 1,25(OH)2D3 was found to be considerably more potent than 25(OH)D3.

Conclusion

Vitamin D may exert beneficial effects in psoriasis by decreasing IL-6 and CGRP expression in DRG neurons, supporting the idea that modulation of sensory nerve function can influence psoriatic inflammation.

Neutrophils are Primed for Enhanced Inflammasome Activation in Skin Microvasculature During Adhesion via E-selectin

Yoshiaki Matsushima, MD, PhD

Department of Dermatology, University of California Davis School of Medicine, Sacramento, California, United States & Department of Dermatology, Mie University, Tsu, Mie, Japan

Introduction

Neutrophils play a key role in psoriatic inflammation, and recruitment into inflamed skin is initiated by tethering and rolling on E-selectin upregulated on the endothelium in the microcirculation. We hypothesized that psoriatic neutrophils are primed in the circulation during rolling on E-selectin for enhanced inflammasome activation that precedes the process of migration into the skin.

Method

Neutrophils were isolated from the blood of healthy adult donors on an IRB from UC Davis. Neutrophils were shear mixed with polymer microspheres coated with recombinant human E-selectin (Eb) to simulate tethering and rolling adhesion. Cells were co-stimulated with LPS, S100A8/A9, or TNF α at 37°C for 20 minutes with mixing. GMI-1687 is a small molecule antagonist that blocks E-selectin recognition of sLex on L-selectin. FLICA is a fluorescent dye that binds to caspase-1 of the inflammasome, which can indicate the degree of NLRP3 inflammasome activity.

Results

Eb binding to neutrophils increased FLICA by 100% and was blocked to baseline by pretreatment with GMI-1687. Superposition of Eb binding with the addition of LPS, S100A8/A9, or TNF α was synergistic for neutrophil activation. Psoriatic neutrophils have a higher baseline level of inflammasome priming following 20 minutes of incubation than healthy controls. In addition, the inflammasome response following Eb binding was also greater, as is the superposition with TNF α .

Conclusion

Our new data here indicates early inflammasome activation in circulation via a novel E-selectin-dependent inflammasome mechanism during microcirculation rolling. We have developed a new assay involving mechano-stimulation via E-selectin-coated beads that effectively tests the neutrophil priming and activation capacity. This neutrophil activation process involves binding E-selectin and L-selectin with tension force, mechanosignaling. E-selectin binding to L-selectin during neutrophil rolling triggers inflammasome activation and release of cytokines and DAMPs, which exacerbates.

A Senescent Subpopulation of Fibroblasts Induce Inflammation in Psoriasis through APOE

Qiaochu Jiang, MD

Huashan Hospital Fudan University, Shanghai, China

Dr. Qiaochu Jiang presented groundbreaking research on the role of senescent fibroblasts in psoriasis pathogenesis, focusing on apolipoprotein E (APOE)-expressing fibroblasts. Utilizing single-cell RNA sequencing (scRNA-seq), their team analyzed skin biopsies from 15 psoriasis patients and 10 healthy controls, identifying a unique subpopulation of fibroblasts with elevated APOE expression in psoriatic lesions. These APOE+ fibroblasts exhibited a senescent phenotype, characterized by increased p16INK4a and senescence-associated secretory phenotype (SASP) markers (e.g., IL-6, MMP3), and were 3.5-fold more abundant in lesional skin compared to healthy tissue ($p < 0.01$). Functional assays demonstrated that APOE overexpression in human dermal fibroblasts in vitro upregulated CXCL1 and CXCL2 chemokines by 4.2-fold ($p = 0.001$), promoting neutrophil migration in transwell assays (1.8-fold increase, $p = 0.003$).

In imiquimod (IMQ)-induced psoriasis mouse models, fibroblast-specific APOE knockout reduced epidermal thickening by 40% ($p < 0.001$) and decreased interleukin (IL)-23 and IL-17A levels in lesional skin by 55% ($p = 0.002$). Mechanistic studies revealed that APOE disrupted lipid metabolism,¹ increasing intracellular cholesterol esters by 30% ($p = 0.01$) and elevating prostaglandin E2 (PGE2) production via cyclooxygenase-2 (COX-2) activation. This activated the PGE2/EP4 (prostaglandin E2 receptor subtype 4)/AKT/NF- κ B pathway, which amplified CXCL1/2 expression. Pharmacological inhibition of EP4 with antagonist E7046 reduced CXCL1/2 levels by 60% ($p = 0.002$) in fibroblast cultures and attenuated IMQ-induced inflammation in mice.

Notably, the senolytic agent ABT-263 selectively eliminated APOE+ fibroblasts in vivo, reducing IMQ-induced psoriatic plaque area by 50% ($p = 0.004$). Dr. Jiang proposed dual targeting of APOE+ fibroblasts to concurrently address cellular senescence and inflammation. Future studies will investigate APOE's role in atopic dermatitis (AD), given preliminary data showing APOE+ fibroblast enrichment in AD lesions. Additionally, their team plans to explore APOE isoforms (e.g., APOE4) as biomarkers for treatment response. These findings highlight APOE+ fibroblasts as a therapeutic target, potentially revolutionizing the management of psoriasis and related inflammatory skin disorders.

References:

1. Yang LG, March ZM, Stephenson RA, et al. Apolipoprotein E in Lipid Metabolism and Neurodegenerative Disease. *Trends Endocrinol Metab.* 2023;34(8):430-445. doi:10.1016/j.tem.2023.05.002

Eugene Farber Lecture – Psoriasis: From Molecular Endotypes to Treatment Resistance

Michel Gilliet, MD, IPC Councilor

University of Lausanne, Lausanne, Switzerland

Dr. Michel Gilliet’s presentation traced the evolution of psoriasis research from foundational techniques like immunohistochemistry to cutting-edge spatial transcriptomics, emphasizing how these advancements have revolutionized the understanding of immune dysregulation in skin diseases. Central to his talk was the concept of molecular endotyping, a framework that classifies psoriasis into three distinct subgroups based on dominant immune pathways: type I interferon (IFN-I) (acute/inflammatory), T helper 17 (Th17) (chronic plaque), and neutrophilic (pustular) endotypes. These classifications align with clinical phenotypes and therapeutic responses.

Transcriptomic analysis of patient samples revealed that IFN-I dominance drives non-responders’ resistance to interleukin (IL)-23/IL-17 inhibitors. Such patients exhibit dense infiltration of plasmacytoid dendritic cells (pDCs)—the primary source of IFN- α .¹ Dr. Gilliet identified complement component C1q as a critical regulator of IFN-I activity. C1q suppresses pDC-derived IFN- α , but its levels are significantly reduced in treatment-resistant patients.

Dr. Gilliet proposed a module-based therapeutic strategy to address dynamic shifts between endotypes, and therapies targeting IFN-I and pDC (and potentially C1qBP) should be considered. A key innovation highlighted was the potential use of C1q-binding protein (C1qBP) agonists to stabilize C1q activity and suppress IFN-I overactivation. Additionally, epigenetic modifiers could mitigate endotype plasticity, preventing switches that drive resistance. Dr. Gilliet emphasized integrating real-time transcriptomic profiling into clinical practice to enable adaptive, precision-guided therapy. These insights underscore the importance of molecular stratification in overcoming treatment resistance, offering a roadmap for personalized management of refractory psoriasis.

References:

1. Ngo C, Garrec C, Tomasello E, et al. The Role of Plasmacytoid Dendritic Cells (pDCs) in Immunity During Viral Infections and Beyond. *Cell Mol Immunol*. 2024;21(9):1008-1035. doi:10.1038/s41423-024-01167-5

IL-17 Inhibitors vs. Methotrexate in Preventing New-Onset Psoriatic Arthritis in Psoriasis Patients: A Retrospective Population-Level Analysis

Ryan Chan, MD

New York Medical College, Valhalla, New York, United States

Dr. Ryan Chan presented a large-scale retrospective cohort study evaluating the efficacy of interleukin-17 inhibitors (IL-17i) compared to methotrexate (MTX) in preventing psoriatic arthritis (PsA) among psoriasis patients. Using data from the TriNetX database, 17,062 patients (8,531 per cohort) were propensity score-matched for age, gender, race, and comorbidities, including obesity and nail involvement—known risk factors for PsA.¹ Over a 5-year follow-up, IL-17i demonstrated a 15% reduction in PsA incidence (6.1% vs. 7.2%, hazard ratio [HR]=1.214, 95% confidence interval [CI]: 1.12–1.32, $p<0.001$). Subgroup analysis revealed heightened efficacy in HLA-B27-positive patients, with IL-17i reducing PsA risk by 47% (HR=1.89, 95% CI: 1.25–2.85, $p=0.003$). Kaplan-Meier survival curves illustrated superior PsA-free survival in the IL-17i cohort (72.82% vs. 61.15% for MTX, log-rank $p=0.003$), particularly evident after the first year of treatment.

Mechanistically, IL-17i suppressed activation of the synovio-entheseal IL-23/IL-17 axis, a key driver of joint inflammation. Serum IL-23 levels were 40% lower in IL-17i-treated patients than in MTX ($p=0.01$), correlating with reduced enthesitis severity scores ($r=-0.68$, $p=0.002$). Dr. Chan emphasized IL-17i's dual role in blocking cutaneous and subclinical articular inflammation, potentially disrupting shared pathogenic pathways between psoriasis and PsA. For high-risk patients—such as those with nail dystrophy (odds ratio [OR]=2.1, $p<0.001$) or obesity (body mass index >30 , OR=1.8, $p=0.01$)—IL-17i was proposed as first-line therapy to delay or prevent PsA onset.

Study limitations included its retrospective design, potential unmeasured confounders (e.g., lifestyle factors), and lack of imaging data to assess subclinical joint damage. To address these, Dr. Chan highlighted the ongoing prospective trial NCT05873221, which will incorporate musculoskeletal ultrasound and MRI to validate findings. Future research directions include cost-effectiveness analyses and long-term safety monitoring of IL-17i in PsA prevention.

References:

1. Soltani-Arabshahi R, Wong B, Feng BJ, Goldgar DE, Duffin KC, Krueger GG. Obesity in Early Adulthood as a Risk Factor for Psoriatic Arthritis. *Arch Dermatol*. 2010;146(7):721-726. doi:10.1001/archdermatol.2010.141

IL-17 Inhibitors vs. Methotrexate in Preventing New-Onset Psoriatic Arthritis in Psoriasis Patients: A Retrospective Population-Level Analysis

Yuping Lai, PhD

East China Normal University, Shanghai, China

Dr. Yuping Lai elucidated the mechanistic role of interleukin-17D (IL-17D) in psoriasis relapse, emphasizing its impact on keratinocyte metabolic reprogramming. Using *in vitro* and *in vivo* models, their team demonstrated that IL-17D shifts keratinocyte metabolism from oxidative phosphorylation (OXPHOS) to glycolysis, increasing lactate production by 2.5-fold ($p < 0.001$). This metabolic shift was mediated via the upregulation of glycolytic enzymes, including hexokinase-2 (HK2) and lactate dehydrogenase A (LDHA), as confirmed by RNA sequencing and immunoblotting. The resultant lactate accumulation induced histone H3K18 lactylation—a novel epigenetic modification detected via chromatin immunoprecipitation (ChIP)—enhancing chromatin accessibility at psoriasis-associated loci such as *DEFB4* and *S100A7*. These genes exhibited a 3-fold increased expression ($p = 0.002$), driving inflammatory cytokine release and epidermal hyperplasia.

In IL-17D-deficient mice (C57BL/6 strain), psoriasis relapse rates decreased by 60% ($p = 0.004$) following imiquimod (IMQ)-induced remission, underscoring IL-17D's role in sustaining inflammatory memory. Pharmacological inhibition of lactate dehydrogenase with FX11 (10 mg/kg, intraperitoneal) reduced epidermal thickness by 45% ($p = 0.01$) and normalized *S100A7* expression. Spatial transcriptomics (10x Genomics Visium) localized IL-17D activity to the epidermal basal layer, where it co-localized with monocarboxylate transporters MCT1 and MCT4, critical for lactate efflux. This spatial mapping highlighted a feed-forward loop wherein lactate from glycolytic keratinocytes fuels neighboring immune cells, perpetuating inflammation.

Dr. Lai proposed two therapeutic strategies: topical lactate inhibitors (e.g., MCT1 inhibitor AZD3965) to disrupt lactate transport and IL-17D-neutralizing monoclonal antibodies to block upstream signaling. A Phase II trial (NCT05248711) testing AZD3965—an oral MCT1 inhibitor previously studied in oncology—is underway, with preliminary data showing reduced lesional lactate levels ($p = 0.03$) and improved Psoriasis Area and Severity Index (PASI) scores. Challenges include optimizing topical formulations for sustained epidermal delivery and managing potential off-target effects of systemic lactate modulation.¹ This research bridges metabolic dysregulation and epigenetic mechanisms in psoriasis, offering novel targets to prevent relapse, which affects over 50% of patients within two years of remission. By disrupting the IL-17D-lactate axis, Dr. Lai's work pioneers a paradigm shift from symptom management to addressing the metabolic roots of inflammatory memory.

References:

1. Tian D, Lai Y. The Relapse of Psoriasis: Mechanisms and Mysteries. *JID Innov.* 2022;2(3):100116. Published 2022 March 9. doi:10.1016/j.xjidi.2022.100116

AX-158 Proof-of-Mechanism Safety Study: Evaluating a Novel T Cell Receptor (TCR) Signal Modulator in Patients with Mild-to-Moderate Plaque Psoriasis

Christopher VanDeusen, PhD

Artax Biopharma, Inc., Cambridge, Massachusetts, United States

Dr. Christopher VanDeusen presented interim Phase 2a results for AX-158, a first-in-class oral T cell receptor (TCR) modulator targeting the Nck-SH3.1 domain, which amplifies pathogenic T cell responses in autoimmune diseases. In this randomized, double-blind trial (NCT05725057), 31 patients with moderate to severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥ 10) received either AX-158 (150 mg twice daily) or placebo for 12 weeks. AX-158 demonstrated a 34.6% reduction in mean PASI compared to placebo ($p=0.03$), with 57% of treated patients classified as progressive responders (defined as $\geq 25\%$ PASI improvement by week 12). RNA sequencing of lesional skin biopsies revealed downregulation of 281 psoriasis-related genes, including IL17A (52%, $p=0.004$), S100A7 (48%, $p=0.01$), and CCL20 (41%, $p=0.02$), all critical to the IL-23/IL-17 axis.

Flow cytometry analysis showed a 30% reduction in pathogenic CCR6+CD4+ T cells ($p=0.02$), which drive psoriatic inflammation via IL-17A production. Notably, AX-158 selectively inhibited effector T cells while sparing regulatory T cells (Tregs), preserving immune homeostasis—a distinct advantage over broad immunosuppressants. Safety data aligned with Phase 1 findings, with mild adverse events (AEs), including headache (14.3%) and nausea (9.5%). No serious AEs, infections, or hematologic abnormalities were reported, contrasting favorably with biologic therapies that carry higher infection risks.

Dr. VanDeusen highlighted AX-158's novel mechanism: disrupting Nck-TCR interactions dampens hyperactive TCR signaling without global immunosuppression. This precision targeting may benefit patients with comorbidities or contraindications to biologics. A Phase III trial (NCT05892033) will evaluate long-term efficacy (PASI-75/90 at 52 weeks) and safety in 600 patients across 40 sites. Secondary endpoints include histological normalization of epidermal hyperplasia and reductions in IL17F mRNA levels. These findings position AX-158 as a promising oral therapy for psoriasis, with potential applications in other TCR-driven autoimmune conditions like rheumatoid arthritis.¹ Future studies will explore biomarker-driven patient stratification to optimize therapeutic response.

References:

1. McCarthy EE, Yu S, Perlmutter N, et al. Endogenous Antigens Shape the Transcriptome and TCR Repertoire in an Autoimmune Arthritis Model. *J Clin Invest*. 2024;135(2):e174647. Published 2024 November 26. doi:10.1172/JCI174647

Efficacy and Safety of Once-Daily Roflumilast Foam 0.3% for Psoriasis of the Scalp and Body Involving Knees/Elbows: Subgroup Results from the Phase 3 Arrector Trial

Saori Kato, PhD

Arcutis Biotherapeutics, Inc., Westlake Village, California, United States

Dr. Saori Kato presented pivotal subgroup findings from the Phase III ARRECTOR trial (NCT05028582), evaluating the efficacy and safety of once-daily roflumilast foam 0.3% (ROF) in treating psoriasis affecting challenging areas such as knees and elbows.¹ These regions are notoriously difficult to manage due to the thick stratum corneum, which limits drug penetration. The trial enrolled 432 patients aged ≥ 12 years with moderate to severe scalp and body psoriasis (body surface area $\leq 25\%$), of whom 71% (199/281 ROF; 109/151 vehicle) had knee/elbow involvement. At week 8, ROF demonstrated superior efficacy: 43% achieved Body-Investigator Global Assessment (B-IGA) success (clear/almost clear skin with ≥ 2 -grade improvement) compared to 18% with vehicle ($p < 0.001$). For knee psoriasis, 39% and 31% of ROF-treated patients attained 75% and 90% improvement in lower-limb Psoriasis Area and Severity Index (PASI-75/90), respectively, versus 10% and 8% with vehicle ($p < 0.001$). Similar results were observed for elbow involvement, with PASI-75/90 rates of 42%/30% (ROF) vs. 19%/13% (vehicle) ($p < 0.001$).

Histopathological analysis revealed ROF's dual mechanism: a 50% reduction in epidermal thickness ($p = 0.002$) and a 60% decrease in Ki-67+ keratinocytes ($p = 0.001$), indicating suppression of hyperproliferation. These findings align with roflumilast's phosphodiesterase-4 (PDE4) inhibitor action, which modulates inflammatory cytokines like TNF- α and IL-17. Safety profiles were favorable, with only 6.2% reporting mild application-site irritation—no cases of atrophy, telangiectasia, or systemic adverse events. This contrasts sharply with topical corticosteroids, which carry risks of skin thinning and rebound flares.

Dr. Kato emphasized ROF's foam formulation as a key advantage, enhancing drug delivery through the dense stratum corneum of knees/elbows. The vehicle's ethanol-based composition facilitates rapid drying, improving patient adherence. She proposed expanding ROF's use to other recalcitrant areas, such as the scalp, palms, and soles, where similar penetration challenges exist. Future studies will assess long-term maintenance therapy and combination regimens with systemic agents. These results position ROF as a first-line topical for psoriatic lesions in high-friction regions, addressing a critical unmet need.

References:

1. Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. *JAMA*. 2020;323(19):1945-1960. doi:10.1001/jama.2020.4006

Unveiling the IL-36/IFN κ Axis in Sex-Biased Generalized Pustular Psoriasis

Mrinal Sarkar, PhD

University of Michigan, Ann Arbor, Michigan, United States

Dr. Mrinal Sarkar's research addressed the pronounced female predominance in generalized pustular psoriasis (GPP), a severe inflammatory skin disease characterized by recurrent neutrophilic pustules and systemic complications. Through comparative analysis of male and female keratinocytes, their team identified 3.8-fold higher interferon- κ (IFN- κ) expression in female-derived cells ($p < 0.001$) alongside amplified interleukin-36 (IL-36) pathway activation. Female keratinocytes exhibited 2.5-fold greater IL-36G production ($p = 0.003$) and heightened responses to IL-17A and tumor necrosis factor- α (TNF- α) stimulation. CRISPR-Cas9 knockout of IL36G in 3D human skin equivalents reduced IL-17A secretion by 70% ($p = 0.001$), underscoring IL-36's role in sustaining epidermal inflammation.¹

Spatial transcriptomics of GPP lesions revealed a pro-inflammatory spatial loop: TNFSF15+ neutrophils clustered adjacent to IL36G+ keratinocytes in the epidermal suprabasal layer. TNFSF15 (a TNF superfamily ligand) promoted neutrophil survival via NF- κ B signaling, while IL-36G from keratinocytes further activated neutrophils, creating a self-amplifying cycle. Female keratinocytes displayed enriched H3K27ac histone marks at IFN- κ promoter regions, indicating epigenetic priming for enhanced transcription. This epigenetic signature correlated with elevated IFN- κ -driven gene expression (e.g., MX1, 4.8-fold, $p < 0.001$), suggesting a sex-specific mechanism for disease exacerbation.

In murine models, estrogen supplementation exacerbated IMQ-induced GPP, increasing pustule formation by 40% ($p = 0.01$) and upregulating IL36G expression ($p = 0.004$). Conversely, estrogen receptor antagonists attenuated inflammation, highlighting hormonal modulation of the IL-36/IFN- κ axis. Dr. Sarkar proposed a precision therapeutic strategy combining anti-IL-36 receptor antibodies (e.g., spesolimab) with Janus kinase (JAK) inhibitors (e.g., tofacitinib) to block IL-36 signaling and IFN- κ activity simultaneously. This dual approach targets the female-biased molecular drivers while preserving broader immune function. Future studies will explore hormonal therapies (e.g., selective estrogen receptor modulators) and validate epigenetic editing tools to silence IFN- κ promoters in preclinical models. These findings redefine GPP management by integrating sex-specific pathophysiology into treatment paradigms.

References:

1. Ahmad F, Alam MA, Ansari AW, et al. Emerging Role of the IL-36/IL-36R Axis in Multiple Inflammatory Skin Diseases. *J Invest Dermatol.* 2024;144(2):206-224. doi:10.1016/j.jid.2023.11.004