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Cytokines as Therapeutic Targets for Inflammatory Acne Valgaris

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Abstract: Acne vulgaris is a chronic disease that affects the pilosebaceous units and is driven by sebum quality, keratinization of follicles, microorganisms, and the immune system. The *Cutibacterium acnes* (*C. acnes*) bacterium is abundant on both healthy and acne-prone skin; its pathogenicity therefore reflects strain-level virulence, community dysbiosis and a permissive follicular microenvironment rather than bacterial abundance alone. *C. acnes* can activate Toll-like receptor 2 (TLR2)-nuclear factor kappa B (NF-κB) and cluster of differentiation 36 (CD36)-reactive oxygen species (ROS) signaling in keratinocytes, TLR2 signaling in sebocytes and monocyte/macrophage-lineage cells, and nucleotide-binding oligomerization domain (NOD)-like receptor family pyrin domain-containing 3 (NLRP3)-caspase-1 processing of interleukin (IL)-1 beta (IL-1β). IL-1, IL-6, IL-8 and tumor necrosis factor alpha (TNF-α) initiate and amplify innate inflammation, whereas IL-12, IL-17 and interferon gamma (IFN-γ) sustain T helper 1 (Th1) and T helper 17 (Th17) responses. Existing guidelines favor benzoyl peroxide (BPO), topical retinoids, and specific antimicrobial approaches. However, these treatment modalities are not alike in terms of impact on microorganism flora. Probiotic and postbiotic strategies demonstrate promising results in clinical trials, while phage therapy, endolysins, and cytokine inhibition are still experimental. This review summarizes *C. acnes*-driven inflammatory signaling, evaluates the microbiome effects of current treatments and identifies priorities for future therapeutic development.

1. Introduction

Acne vulgaris is one of the most common forms of dermatological conditions with prevalence rates of around 9% worldwide and 85% among adolescents and young adults. Although it is not life-threatening, acne can cause permanent scarring and a substantial psychosocial burden [1]. Acne vulgaris is an inflammatory condition affecting the pilosebaceous unit. The well-known pathogenic factors in the disease are excess or abnormal production of sebum, hyperkeratinization of the follicular infundibulum, mocrobial dysbiosis, and host immune inflammation. It is important to note that these factors are not separate etiological factors but are rather part of an ecological immune system where the microenvironment of the follicle influences specific microbial functions, and host immune inflammation remolds the and generates a positive feedback loop [2,3].

Within this systems framework, the role of *C. acnes* requires reconsideration. As a dominant commensal in sebum-rich skin, *C. acnes* contributes to maintenance of an acidic surface environment and colonization resistance under homeostatic conditions. However, total bacterial abundance alone does not distinguish health from disease because *C. acnes* is abundant in both healthy skin and acne lesions. Pathogenicity is more closely associated with disruption of phylotype balance, enrichment of specific lineages and strain-to-strain differences in inflammatory potential than with a simple increase in bacterial load [4,5]. Recent isolate-level analyses further showed marked differences in inflammatory capacity even among closely related strain types; acquisition of accessory genetic elements may contribute to this heterogeneity, underscoring the functional limitations of genus- or species-level measurements [6]. These findings support a model in which *C. acnes* pathogenicity depends on the interplay between strain-level variation in virulence and host responses shaped by the local follicular microenvironment [4].

This review uses strain heterogeneity and microenvironmental dependence as an organizing framework to examine follicular ecology, innate immune sensing, adaptive immune amplification, cytokine networks and targeted therapy. It summarizes the molecular mechanisms by which *C. acnes* initiates and amplifies immune inflammation in acne and evaluates how different therapeutic strategies remodel the follicular microbiome, thereby informing the development of interventions that preserve cutaneous microbial homeostasis.

2. Follicular Microenvironment and Cutaneous Dysbiosis

The pilosebaceous unit is a lipid-rich and relatively anaerobic ecological niche. Increased sebum production and altered lipid composition, together with abnormal keratinization, promote microcomedone formation and modify nutrient availability, oxygen tension and the diffusion of microbial products . These changes can favour biofilm formation and the growth of disease-associated *C. acnes* phylotypes, while obstruction of the follicular ostium retains antigens and pro-inflammatory lipids locally. Conversely, homeostatic *C. acnes* populations can generate free fatty acids that help maintain an acidic skin surface and exclude other potential pathogens. C. acnes is therefore better regarded as a context-dependent commensal pathobiont than as an obligate pathogen [7,8].

Acne-associated dysbiosis cannot be summarized by microbial diversity alone. Studies differ substantially in sampling site, lesion stage, previous treatment, sequencing region and taxonomic resolution, and surface swabs may not accurately represent the follicular interior. Nevertheless, recent reviews converge on three conclusions: strain/phylotype composition is more informative than total *C. acnes* abundance; interactions with staphylococci and other community members influence homeostasis; and acne treatments themselves can alter microbial-community composition [3-5]. A 2023 randomized exploratory study found that topical retinoic acid (VAA) and BPO significantly reduced bacterial diversity at month 1, while a dermocosmetic product (DC) did not. Notably, the DC group was associated with an increase in relative abundance of *Cutibacterium* and decrease in relative abundance of *Staphylococcus*, while VAA and BPO displayed a reverse effect, suggesting that different medications affect the skin microbial community differently in mild acne patients [9].

Excess and compositionally abnormal sebum favors organisms with high lipase activity. Microbial lipases hydrolyze triglycerides into free fatty acids, which may promote keratinocyte hyperproliferation and differentiation and thereby aggravate follicular hyperkeratinization. Keratinization narrows the follicular opening, increases retention of follicular contents and prolongs local exposure to microbial products. Once inflammation begins, edema, lipid oxidation and tissue injury further alter the niche. Follicular ecology, microbial composition and host inflammation therefore form a bidirectional feedback loop [10]. The same strain may be well tolerated in an open, homeostatic follicle but become inflammatory in a lipid-rich, obstructed follicle; conversely, similar

lesion phenotypes may arise from different combinations of microbial and host factors.

3. C. acnes-Mediated Inflammatory Signalling and the Cytokine Network

3.1 C. acnes-Mediated Innate Immune Activation

Keratinocytes are sentinel cells at the follicular interface. Recognition of *C. acnes* is mediated predominantly by TLR2, although TLR4 activation has also been reported in keratinocytes. These receptors promote NF-κB-dependent transcription of IL-1, IL-6, IL-8, TNF-α, granulocyte-macrophage colony-stimulating factor (GM-CSF), human beta-defensin 2 (hBD-2) and matrix metalloproteinases (MMPs) [11]. CD36-dependent recognition can additionally generate ROS. Together, these pathways lead to barrier inflammation: IL-8 attracts neutrophils, TNF-α and IL-1 increase endothelial and epithelial activation, and MMPs may cause damage and scarring.

Sebocytes and the cell types derived from monocyte/macrophage lineage also participate in this inflammatory cascade. The activation of TLR2-NF-κB results in the expression of IL-8 and IL-12, while *C. acnes* primes the NLRP3 and caspase-1 to allow for the conversion of pro-IL-1β to active IL-1β. Therefore, IL-1β acts as both a downstream effector of pathogen detection and an activator of keratinocytes and leukocytes. Experimental evidence shows that *C. acnes* activates IL-1β by means of the NLRP3 inflammasome. However, the exact profile of this pathway in human acne spots still needs to be determined [12]. One of the defining features of the model is convergence of pathways: different host cells can sense microbes and lipids via distinct receptors but all work to create a pro-inflammatory microenvironment.

Secreted virulence factors may potentiate these signaling molecules. Lipases affect the lipid content of the hair follicle, hyaluronidases may assist in extracellular-matrix degradation, and Christie-Atkins-Munch-Petersen (CAMP) factors and porphyrin-induced oxidative stress have been associated with inflammatory activity [5,6,13]. Expression of these molecules depends on the strain and the physiological state of the bacteria, which partially explains why the number of bacteria cannot be correlated with the severity of the disease. An informative biomarker would need to integrate information about the strain or the virulence gene expression together with host-response readout rather than treating all *C. acnes* as functionally equivalent.

3.2 Th1/Th17- and Neutrophil-Mediated Inflammatory Amplification

Innate immune responses create the cytokine milieu that is necessary for recruiting and polarizing T cells. The stimulation of PBMCs by *C. acnes* causes the secretion of IL-6, IL-1β and transforming growth factor beta (TGF-β), which results in the differentiation of naive cluster of differentiation 4-positive (CD4+) T cells into Th17 cells, whereas IL-12 is responsible for Th1 polarization. IL-17 and IFN-γ production leads to increased production of chemokines and further inflammatory response [11,14,15]. The acne-related strains cause more IL-17 production compared to strains of healthy skin, providing a mechanistic link between strain ecology and lesion inflammation. Recent literature indicates that Th17 pathway plays a role in the early events of immune response to acne rather than just being involved in the secondary response [14,16].

The neutrophils are especially abundant in papules and pustules. The IL-8 is the source of the direct chemotactic signal. Moreover, vascular endothelial growth factor-alpha (VEGF-α) secreted from conventional type 1 dendritic cell (cDC1) has also been proposed to be an alternate pathway linking bacterial load locally with the neutrophil migration and altered neutrophil phenotypes [17]. In contrast, the cDC1 pathway is based on experimental studies of skin infection by bacteria and has been tested in acne populations to a lesser extent than the TLR2 and Th17 pathways. Thus, it should be regarded as a potential amplification pathway rather than as a proven core mechanism in acne.

Neutrophilic proteases and ROS are able to eliminate bacteria but also to impair the follicular wall and to allow inflammation to extend into the dermis.

These reactions vary with the stage of lesion and are not always damaging. Th17 cells can contribute to commensal control, whereas an excessive or persistent IL-17 program in an obstructed follicle may promote epithelial chemokine production and sustained neutrophil infiltration. Similarly, neutrophils are protective during microbial invasion, but degranulation and oxidative responses within a confined pilosebaceous unit may cause tissue injury [18]. Immune cells and cytokines therefore have both protective and pathogenic functions in acne, and simple depletion of a cell population or complete blockade of a single cytokine may not translate into clinical benefit.

3.3 Key Cytokines and Their Interrelationships

The acne cytokine network can be simplified into initiation, recruitment and persistence modules. IL-1α and IL-1β connect abnormal keratinization with inflammation and provide feed-forward activation of keratinocytes and myeloid cells. IL-6 contributes to acute inflammation and, together with IL-1β and TGF-β, promotes Th17 differentiation. IL-8, also known as C-X-C motif chemokine ligand 8 (CXCL8), is the major neutrophil chemoattractant produced by keratinocytes, sebocytes and monocytes. TNF-α reinforces NF-κB signaling, endothelial activation and tissue inflammation. IL-12 promotes Th1/IFN-γ activity, whereas IL-17 induces epithelial chemokines and antimicrobial programs and can act synergistically with TNF-α [11,13-15].

Feedback links these modules. IL-1β and IL-6 promote Th17 differentiation; IL-17 returns the signal to the follicular epithelium by enhancing chemokine and antimicrobial programs; IL-8 recruits neutrophils that release proteases and ROS; and the ensuing tissue injury exposes additional microbial and damage-associated signals. TNF-α can cooperate at several steps, while IL-12 and IFN-γ maintain a parallel Th1 arm. This interconnected network better explains persistent papules and pustules than any single cytokine acting independently (Figure 1).

The network structure also clarifies therapeutic priorities. TLR/NF-κB is an upstream hub that controls several downstream responses, but systemic blockade could impair host defense. NLRP3-IL-1β and Th17-IL-17 are relatively selective inflammatory amplifiers and are therefore attractive targets; however, direct neutralization of these pathways has not yet established a favorable acne-specific benefit-risk or cost-effectiveness profile. IL-8 is mechanistically close to pustule formation, but neutrophil chemotactic signals are redundant. Biomarker studies should therefore assess functional pathway combinations at lesion level, such as NLRP3/IL-1β with IL-8 or IL-17 with epithelial chemokines, rather than measuring a single circulating cytokine.

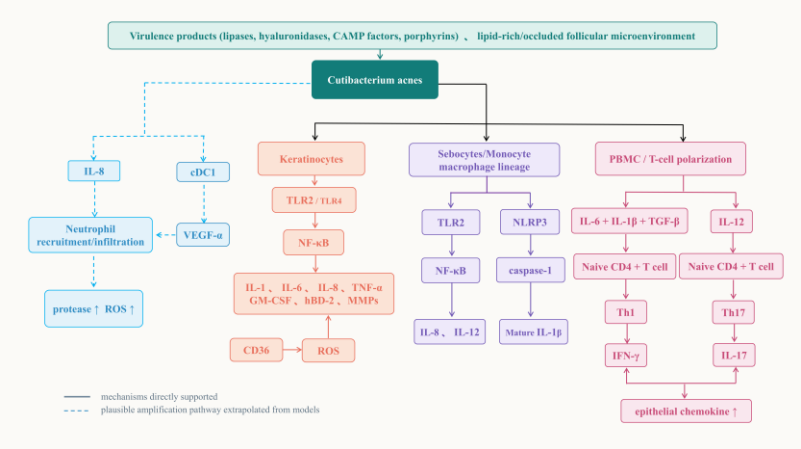

Figure 1: C. acnes–Mediated Inflammatory signalling and the Cytokine Network.

4. Microbiome- and Host-Directed Therapy: Evidence Levels

The 2024 American Academy of Dermatology guideline strongly recommends BPO, topical retinoids, topical antibiotics and oral doxycycline, and strongly recommends isotretinoin for severe acne, acne at risk of scarring, disease causing substantial psychosocial burden or treatment-refractory acne [19]. Within this framework, good clinical practice also favors combining topical agents with different mechanisms, limiting courses of systemic antibiotics and using antibiotics with a non-antibiotic topical treatment. These regimens have greater clinical certainty than any microbiome-selective or cytokine-targeted strategy. The relative evidence levels and clinical interpretation of established, microbiome-directed, and host-directed therapies are summarized in Table 1. From a microbiome-preservation perspective, BPO provides non-antibiotic antimicrobial activity; retinoids correct follicular keratinization and disrupt the obstructed inflammatory niche; and isotretinoin acts further upstream by markedly reducing sebum.

Microbiome-directed strategies aim to restore function rather than sterilize the follicle. Topical or oral probiotics and postbiotics may inhibit *C. acnes*, modify microbial communities, improve barrier function or reduce inflammatory mediators. Recent small randomized controlled trials (RCTs) suggest that probiotic-derived lotion, oral probiotic combinations, probiotics used with isotretinoin or probiotics added to conventional therapy may reduce inflammatory lesions [20-23]. However, strains, formulations, comparators and outcomes differ substantially, and a systematic review concluded that the results, although promising, remain insufficient to replace guideline-supported standard therapy [24]. Phages and endolysins may selectively eliminate specific *C. acnes* strains while preserving commensals, but delivery, resistance or tolerance, follicular penetration, formulation stability and safety remain unresolved; current evidence is predominantly preclinical or early translational [25,26].

Host-directed approaches may attenuate the same network without relying on broad-spectrum antibacterial activity. Retinoids normalize keratinization, regulate sebum secretion and composition, and reduce TLR2-mediated responses. All-trans retinoic acid (ATRA) can also induce tumor necrosis factor alpha-induced protein 3-interacting protein 1 (TNIP1), a negative regulator of NF-Kb [27,28]. Nitric oxide (NO)-releasing nanoparticles reduced both C. acnes burden and IL-1β, TNF-α, IL-6 and IL-8 in experimental systems [29].

Direct blockade of IL-1 or IL-17 is mechanistically attractive, but a placebo-controlled pilot trial of anti-IL-17A therapy did not significantly reduce inflammatory lesions [30]. This negative result demonstrates that pathway activation does not necessarily predict therapeutic efficacy. Signal redundancy, lesion stage and patient selection may determine whether a cytokine is causal, compensatory or merely associated. On current evidence, retinoids and non-antibiotic standard treatments are clinically established; probiotics remain adjunctive and investigational; and phage/endolysin, inflammasome-directed and cytokine-biologic approaches remain exploratory.

Table 1. Evidence levels for microbiome- and host-directed acne therapies.

Strategy	Evidence level	Interpretation
BPO, topical retinoids and combination regimens	High	Guideline-supported core treatment; non-antibiotic options reduce resistance-selection pressure [19].
Systemic antibiotics	High efficacy;	Use in selected moderate-to-severe disease; limit treatment duration and combine with topical therapy [19].

	stewardship limitation	
Oral isotretinoin	High	Strongly recommended for severe, scarring or refractory acne; safety monitoring is required [19].
Topical or oral probiotics/postbiotics	Low	Several small RCTs and a systematic review; strains, formulations and endpoints are heterogeneous [20-24].
Phages/endolysins or NO-releasing nanoparticles	Very low	Selective or combined antimicrobial and anti-inflammatory concepts; evidence remains preclinical or early translational [25,26,29].
Direct IL-1/IL-17 or inflammasome targeting	Very low	Mechanistically plausible; an anti-IL-17A pilot trial was negative and IL-1/NLRP3 efficacy is unproven [12,30].

5. Conclusions

Current evidence is limited by heterogeneous sampling methods, extensive reliance on surface swabs, inadequate strain resolution, predominantly cross-sectional designs, limited longitudinal follow-up and inconsistent lesion phenotyping. Relative abundance can change without a corresponding change in absolute bacterial load, while 16S ribosomal RNA (16S rRNA) gene sequencing cannot reliably resolve virulence genes or microbial activity. Treatment studies rarely integrate strain-resolved metagenomics, transcriptomics, cytokine measurements and standardized clinical endpoints. *In vitro* stimulation and intradermal mouse models also use bacterial doses and tissue contexts that differ from naturally obstructed human follicles [3,4,6].

Future translational research should longitudinally sample matched non-lesional skin, comedonal lesions and inflammatory follicles from the same patient; quantify absolute microbial loads; conduct strain-level genomic and functional analyses; and prespecify cytokine modules. Trials of probiotics, phages and postbiotics should report strain identity, viability, formulation, antibiotic exposure and the durability of microbiome changes. Treatment selection may ultimately depend on whether a patient's disease is dominated by altered sebum biology, hyperkeratinization, inflammatory *C. acnes* strains, Th17 activity or treatment-induced dysbiosis. Stratification according to these dominant drivers is more likely to succeed than a universal microbiome product [31]. Future trials should also distinguish target engagement or biological response from clinical efficacy and should incorporate inflammatory and non-inflammatory lesion counts, scarring risk, patient-reported burden, durability after discontinuation and selection for antimicrobial resistance alongside mechanistic endpoints.

Abbreviations

16S rRNA	16S ribosomal RNA
ATRA	All-trans retinoic acid
BPO	Benzoyl peroxide
C. acnes	*Cutibacterium acnes*
CAMP	Christie-Atkins-Munch-Petersen factor

CD36	Cluster of differentiation 36
CD4+	Cluster of differentiation 4-positive
cDC1	Conventional type 1 dendritic cell
CXCL	C-X-C motif chemokine ligand
DC	dermocosmetic product
GM-CSF	Granulocyte-macrophage colony-stimulating factor
hBD-2	Human beta-defensin 2
IFN	Interferon
IL	Interleukin
MMP	Matrix metalloproteinase
NF-κB	Nuclear factor kappa B
NLRP3	NOD-like receptor family pyrin domain-containing 3
NO	Nitric oxide
PBMC	Peripheral blood mononuclear cell
RCT	Randomized controlled trial
ROS	Reactive oxygen species
TGF-β	Transforming growth factor beta
Th1	T helper 1
Th17	T helper 17
TLR	Toll-like receptor
TNF-α	Tumor necrosis factor alpha
TNIP1	Tumor necrosis factor alpha-induced protein 3-interacting protein 1
VAA	topical retinoic acid
VEGF-α	Vascular endothelial growth factor alpha

Author Contributions

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References

[1] Eichenfield, D. Z., Sprague, J. & Eichenfield, L. F. Management of Acne Vulgaris: A Review. JAMA-J. Am. Med. Assoc. 326, 2055-2067 (2021).

[2] Tuchayi, S. M. et al. Acne vulgaris. Nat. Rev. Dis. Primers 1, 20 (2015).
[3] Podwojniak, A. et al. Acne and the cutaneous microbiome: A systematic review of mechanisms and implications for treatments. J. Eur. Acad. Dermatol. Venereol. 39, 793-805 (2025).
[4] Dreno, B. et al. Acne microbiome: From phyla to phylotypes. J. Eur. Acad. Dermatol. Venereol. 38, 657-664 (2024).
[5] Dessinioti, C. & Katsambas, A. The Microbiome and Acne: Perspectives for Treatment. Dermatology and Therapy 14, 31-44 (2024).
[6] O'Neill, A. M. et al. Genetic and Functional Analyses of Cutibacterium Acnes Isolates Reveal the Association of a Linear Plasmid with Skin Inflammation. J. Invest. Dermatol. 144, 13 (2024).
[7] van Steensel, M. A. M. The Evolving Microbial Paradigm in Acne. Biomolecules 16, 14 (2026).
[8] Mayslich, C., Grange, P. A. & Dupin, N. Cutibacterium acnes as an Opportunistic Pathogen: An Update of Its Virulence-Associated Factors. Microorganisms 9, 21 (2021).
[9] Wongtada, C. et al. Distinct skin microbiome modulation following different topical acne treatments in mild acne vulgaris patients: A randomized, investigator-blinded exploratory study. Exp. Dermatol. 32, 906-914 (2023).
[10] Lai, Y. et al. Lipase GehA functions as a positive-feedback amplifier of Cutibacterium acnes-sebum interactions in acne pathogenesis. J Invest Dermatol, S0022-0202X(0026)02717-X (2026).
[11] Kim, J. et al. Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. J. Immunol. 169, 1535-1541 (2002).
[12] Qin, M. et al. Propionibacterium acnes Induces IL-1β Secretion via the NLRP3 Inflammasome in Human Monocytes. J. Invest. Dermatol. 134, 381-388 (2014).
[13] Lee, Y. B., Byun, E. J. & Kim, H. S. Potential Role of the Microbiome in Acne: A Comprehensive Review. J. Clin. Med. 8, 25 (2019).
[14] Agak, G. W. et al. Phenotype and Antimicrobial Activity of Th17 Cells Induced by Propionibacterium acnes Strains Associated with Healthy and Acne Skin. J. Invest. Dermatol. 138, 316-324 (2018).
[15] Jin, Z. C., Song, Y. J. & He, L. A review of skin immune processes in acne. Front. Immunol. 14, 12 (2023).
[16] Mias, C., Mengeaud, V., Bessou-Touya, S. & Duplan, H. Recent advances in understanding inflammatory acne: Deciphering the relationship between Cutibacterium acnes and Th17 inflammatory pathway. J. Eur. Acad. Dermatol. Venereol. 37, 3-11 (2023).
[17] Janela, B. et al. A Subset of Type I Conventional Dendritic Cells Controls Cutaneous Bacterial Infections through VEGFα-Mediated Recruitment of Neutrophils. Immunity 50, 1069-1083 (2019).
[18] Mellett, M., Danis, J. & Meier-Schiesser, B. Editorial: Impact of the innate and adaptive immune system in driving type 1 inflammatory skin disease. Front. Immunol. 16, 3 (2025).
[19] Reynolds, R. V. et al. Guidelines of care for the management of acne vulgaris. J. Am. Acad. Dermatol. 90, 30 (2024).
[20] Atefi, N. et al. Evaluating the Effectiveness of Probiotic Supplementation in Combination With Doxycycline for the Treatment of Moderate Acne: A Randomized Double-Blind Controlled Clinical Trial. J. Cosmet. Dermatol. 24, 9 (2025).
[21] Liang, L. L., Qi, X. Y., Jiang, X. K., Chen, T. T. & Dong, L. N. Lactobacillus plantarum MH-301 as an effective adjuvant to isotretinoin in the treatment of acne vulgaris: a randomized and open-label trail. Front. Med. 10, 13 (2024).
[22] Eguren, C. et al. A Randomized Clinical Trial to Evaluate the Efficacy of an Oral Probiotic in Acne Vulgaris. Acta Derm.-Venereol. 104, 6 (2024).
[23] Sathikulpakdee, S. et al. Efficacy of probiotic-derived lotion from Lactobacillus paracasei MSMC 39-1 in mild to moderate acne vulgaris, randomized controlled trial. J. Cosmet. Dermatol. 21, 5092-5097 (2022).
[24] Boby, A., Lee, G., Natarelli, N. & Correa, L. Using probiotics to treat acne vulgaris: systematic review. Archives of Dermatological Research 316, 10 (2024).
[25] Bashir, H. H., Hasnain, M. A. & Moon, G. S. Substrate Specificity and Immunological Implications of Cutibacterium acnes Phage Endolysins. J. Microbiol. Biotechnol. 36, 8 (2026).
[26] Castillo, D. E., Nanda, S. & Keri, J. E. Propionibacterium (Cutibacterium) acnes Bacteriophage Therapy in Acne: Current Evidence and Future Perspectives. Dermatology and Therapy 9, 19-31 (2019).
[27] Erdei, L. et al. TNIP1 Regulates Cutibacterium acnes-Induced Innate Immune Functions in Epidermal Keratinocytes. Front. Immunol. 9, 11 (2018).
[28] Dispenza, M. C. et al. Systemic Isotretinoin Therapy Normalizes Exaggerated TLR-2-Mediated Innate Immune Responses in Acne Patients. J. Invest. Dermatol. 132, 2198-2205 (2012).
[29] Qin, M. et al. Nitric Oxide-Releasing Nanoparticles Prevent Propionibacterium acnes-Induced Inflammation by Both Clearing the Organism and Inhibiting Microbial Stimulation of the Innate Immune Response. J. Invest. Dermatol. 135, 2723-2731 (2015).
[30] Thiboutot, D. M. et al. Anti-IL-17A blockade did not significantly reduce inflammatory lesions in a placebo-controlled pilot study in adult patients with moderate to severe acne. J. Dermatol. Treat. 34, 7 (2023).
[31] Niedzwiedzka, A., Micallef, M. P., Biazzo, M. & Podrini, C. The Role of the Skin Microbiome in Acne: Challenges and Future Therapeutic Opportunities. International Journal of Molecular Sciences 25, 20 (2024).