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A Review of the Pathogenic Mechanisms of Propionibacterium Acnes in Acne

Wenshan Dong

Wuhan University, Wuhan, China
1077212011@qq.com

Abstract: Acne is a common chronic inflammatory skin disease that primarily affects adolescents and young adults, with an incidence rate exceeding 80% in this population. Its pathogenesis is complex and multifactorial, involving excessive sebaceous gland secretion, inflammation, and infection, etc. Among them, Propionibacterium acnes (P. acnes) is considered one of the key pathogenic factors. This paper reviews recent domestic and international research on the pathogenic mechanisms of P. acnes in acne, with a detailed discussion on its biological characteristics, its role in acne pathogenesis, and its interactions with the host immune system. P. acnes triggers and intensifies the inflammatory response of hair follicles and their surrounding tissues through multiple pathways. Additionally, it induces follicular hyper keratinization, promotes biofilm formation, and activates both innate and adaptive immune responses, further exacerbating acne development. By analyzing existing literature, this study aims to provide theoretical support for acne treatment and offer references and practical guidance for future research.

Keywords: Acne, Propionibacterium acnes, Pathogenesis, Inflammatory response, Immune system

1. Introduction

Acne vulgaris is a chronic inflammatory disease primarily affecting the pilosebaceous unit, with a high prevalence, particularly among adolescents, where incidence rates exceed 80% [1]. The pathogenesis of acne is complex and involves multiple factors, including excessive sebaceous gland secretion, abnormal keratinization of the follicular sebaceous duct, P. acnes infection, and inflammatory responses [2]. With the advancement of molecular biology techniques in recent years, P. acnes, a commensal bacterium on the skin surface, has been increasingly recognized for its crucial role in the onset and progression of acne. Studies have shown that the pathogenic mechanisms of P. acnes are multifaceted, encompassing stimulation of sebaceous gland secretion, induction of excessive keratinization in the follicular sebaceous duct, and activation of the host immune response, thereby triggering inflammation [3]. Furthermore, different P. acnes strains exhibit varying degrees of pathogenicity, with Type II strains being more closely associated with acne development [4]. To accurately diagnose acne and develop appropriate treatment strategies, various methods for detecting P. acnes have been developed, including traditional culture methods, polymerase chain reaction (PCR), and high-throughput sequencing [5]. In terms of treatment, sensitive antibiotics combined with retinoids are commonly used [6], while emerging therapies such as photodynamic therapy and laser treatment have also gained attention [7]. With further research into the biological characteristics

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of P. acnes and its interactions with the host immune system, its role in acne pathogenesis has become increasingly clear. This paper reviews the pathogenic mechanisms of P. acnes in acne, aiming to provide new insights for acne prevention and treatment.

2. Biological characteristics of propionibacterium acnes

P. acnes is a Gram-positive anaerobic bacterium, with five confirmed subspecies: Cutibacterium acnes, Cutibacterium avidum, Cutibacterium granulosum, Cutibacterium humerusii (formerly known as Propionibacterium humerusii), and Cutibacterium namnetense [8]. It is widely distributed in the human skin, oral cavity, and intestines, with a particular prevalence in sebaceous gland-rich areas. As a facultative anaerobe, P. acnes thrives in sebum-rich environments containing triglycerides. Its cell wall structure includes various components, such as lipopolysaccharides (LPS), lipoproteins, and peptidoglycans, which play crucial roles in inducing inflammatory responses. Additionally, P. acnes secretes multiple enzymes, including proteases, lipases, and hyaluronidases [9], which decompose triglycerides in sebum, generating free fatty acids that stimulate inflammatory responses in the pilosebaceous unit.

Recent studies have revealed a close relationship between the phylogenetic types of P. acnes and their pathogenicity [4]. Different phylogenetic types exhibit distinct pathogenic mechanisms and clinical manifestations, offering potential for targeted treatments. For instance, IA-type strains are predominantly found on the skin surface and are associated with acne vulgaris, whereas IB/II-type strains are more commonly linked to soft tissue and deep tissue infections [10]. These strain-specific differences pose challenges for acne treatment and have prompted further investigations into the pathogenic mechanisms of different P. acnes strains.

3. Colonization and proliferation of propionibacterium acnes in hair follicles

3.1. Hair follicle microenvironment and colonization of propionibacterium acnes

The hair follicle-sebaceous gland unit is the primary site for the colonization of Propionibacterium acnes. The microenvironment within the hair follicle provides ideal conditions for the growth of P. acnes. Excessive sebum secretion is an important factor in the development of acne, as an excess of sebum serves as a rich nutrient source for P. acnes [11]. Studies have shown that triglycerides in sebum are the primary carbon source for P. acnes, and their breakdown products, free fatty acids, can further stimulate the proliferation of follicular keratinocytes, leading to follicular orifice blockage and the formation of comedones [12].

3.2. Proliferation of propionibacterium acnes and follicular blockage

There is a close relationship between the proliferation of Propionibacterium acnes within the hair follicle and follicular blockage. As the number of P. acnes increases, the accumulation of its metabolic byproducts also rises. These metabolic byproducts can stimulate the abnormal proliferation and excessive keratinization of follicular keratinocytes, further exacerbating follicular orifice blockage. Additionally, P. acnes can induce an inflammatory response in the follicular wall, leading to its rupture and the release of its contents into the surrounding skin tissue, triggering a broader inflammatory reaction.

4. Mechanisms of propionibacterium acnes in acne pathogenesis

Propionibacterium acnes (P. acnes) contributes to acne pathogenesis through multiple pathways, including the induction of inflammatory and immune responses, promotion of follicular sebaceous gland keratinization abnormalities, and biofilm formation.

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4.1. Induction of inflammatory response

P. acnes can induce the release of inflammatory responses through various mechanisms. Its cell wall component, lipopolysaccharide (LPS), can activate immune cells within the hair follicle-sebaceous gland unit, such as macrophages and dendritic cells, which in turn secrete pro-inflammatory cytokines, including interleukin-1α (IL-1α), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). These inflammatory cytokines further recruit neutrophils and other inflammatory cells, exacerbating inflammation in the hair follicle and surrounding tissues [10]. Additionally, P. acnes can activate Toll-like receptors (TLRs), secrete inflammatory mediators, and trigger the activation of the NLRP3 inflammasome [13], further promoting inflammation. Hyaluronidase produced by P. acnes degrades hyaluronic acid and other glycosaminoglycans in skin cells, contributing to acne-related inflammation [14]. Moreover, P. acnes produces porphyrins, which generate reactive oxygen species (ROS) that lead to keratinocyte inflammation and acne lesion formation [5].

4.2. Promotion of follicular sebaceous gland keratinization abnormalities

P. acnes secretes various enzymes and toxins that disrupt the normal keratinization process in the follicular sebaceous duct, leading to the formation of keratin plugs. This process is a critical step in the development of acne comedones [15]. The formation of keratin plugs not only blocks the follicular orifice but also impedes normal sebum excretion, further aggravating follicular inflammation. Additionally, P. acnes metabolic byproducts stimulate abnormal proliferation and excessive keratinization of follicular keratinocytes, exacerbating follicular blockage [16]. Furthermore, membrane proteins, cytoplasmic proteins, and lipoteichoic acid in P. acnes extracts can upregulate the expression of integrins and filaggrin in keratinocytes, further reinforcing keratinization [17].

4.3. Biofilm formation

P. acnes can form biofilms, which are complex structures composed of bacteria, extracellular polymers, and water [18]. The ability to form biofilms is associated with P. acnes virulence, and different P. acnes subtypes exhibit varying degrees of biofilm formation capability [19]. The P. acnes genome encodes several key virulence factors, such as lipases and CAMP factors, which play crucial roles in acne pathogenesis [20]. Studies have further shown that P. acnes biofilms can induce inflammatory responses in human keratinocytes and are closely linked to the activation of the TLR2/MAPK/NF-κB signaling pathway [21]. Biofilm formation enhances P. acnes resistance to the host immune system and antibiotics. Under biofilm protection, P. acnes can evade immune surveillance and clearance, allowing it to persist within the hair follicle and induce sustained inflammation.

4.4. Immune response

The interaction between P. acnes and the host immune system is a crucial aspect of acne pathogenesis. This interaction involves both the activation and evasion mechanisms of P. acnes and the immune system's response and regulation.

Under the influence of specific cytokines and antigen-presenting cells, naive CD4+ T cells can differentiate into various T-cell subtypes. Among them, Th17 cells and their secretion of IL-17 play a role in both adaptive and innate immunity by defending against pathogens. However, excessive activation of Th17 cells can lead to inflammatory diseases, including acne [22]. Certain P. acnes components can activate CD4+ T cells through the TLR2 signaling pathway, promoting their differentiation into Th17 cells, which then produce IL-17 and other inflammatory cytokines, driving acne development [23].

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4.4.1. Innate immune response

P. acnes can activate the host's innate immune response. Its cell wall components are recognized by pattern recognition receptors (PRRs) in the host, such as Toll-like receptor 2 (TLR2) and NOD-like receptors (NLRs), which activate downstream signaling pathways, leading to the release of inflammatory mediators and the infiltration of immune cells [24]. Additionally, P. acnes induces immune cells in the hair follicle-sebaceous gland unit to secrete antimicrobial peptides such as β-defensins and LL-37. These antimicrobial peptides can inhibit P. acnes growth but may also stimulate inflammatory responses [25].

4.4.2. Adaptive immune response

P. acnes also triggers the host's adaptive immune response. Its antigenic components can be taken up and presented by dendritic cells, activating B cells and T cells, resulting in the production of specific antibodies and the initiation of cellular immune responses. While adaptive immunity can contribute to the clearance of P. acnes infection, immune system dysfunction can lead to excessive immune reactions, worsening acne severity.

5. Research prospects

Propionibacterium acnes (P. acnes) plays a crucial role in the pathogenesis of acne. Scholars both in China and abroad have conducted in-depth studies on the biological characteristics of P. acnes, its pathogenic mechanisms, and its interactions with the host immune system, yielding significant findings. These studies have provided strong support for the prevention and treatment of acne. However, several issues and challenges remain. For instance, the pathogenic mechanisms of P. acnes have yet to be fully elucidated, and differences in virulence among different strains require further investigation. Additionally, acne development is influenced by host factors, but the mechanisms underlying the interaction between these factors and P. acnes remain unclear, limiting a comprehensive understanding of acne pathogenesis. Moreover, the widespread use of antibiotics has led to an increasing problem of antibiotic resistance in P. acnes, posing new challenges for acne treatment.

Research on the pathogenic mechanisms of P. acnes is crucial for developing effective acne treatments. With the extensive use of antibiotics in acne treatment, antibiotic resistance in P. acnes has become increasingly severe. Studies have shown that in certain regions, the resistance rate of P. acnes to macrolide antibiotics has risen significantly, with resistance mechanisms involving point mutations in the 23S rRNA gene and horizontal transfer of the erm gene [26–28]. Future research should focus on dynamic monitoring of resistance gene distribution, optimizing antibiotic usage guidelines, and developing novel antimicrobial agents (such as antimicrobial peptides and phage therapy) to overcome resistance. At the same time, integrating research on the skin microbiome may provide new perspectives on acne treatment. To address imbalances in the skin microbiome, various microbiome-based therapeutic strategies have been proposed, including the use of probiotics and microbiota modulation, offering potential alternatives to antibiotic-based treatments [29].

Based on current research progress and challenges, future studies should focus on the following aspects. First, further exploration of the pathogenic mechanisms of P. acnes is needed, particularly regarding the differences in virulence among different strains, to provide a theoretical foundation for developing more effective treatments. Techniques such as genome sequencing and strain typing can be used to reveal genetic variations and pathogenic potential among different strains. Second, more attention should be given to the influence of host factors, including individual genetic background, hormone levels, and immune status, to elucidate the mechanisms underlying P. acnes-host interactions. This would help clarify the role of host factors in acne pathogenesis and provide

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theoretical and practical guidance for personalized treatment. Additionally, interdisciplinary collaboration should be strengthened. The pathogenesis of acne is highly complex, involving multiple disciplines such as microbiology, immunology, and dermatology. Future research should promote interdisciplinary cooperation, employing diverse research methods to gain deeper insights into acne pathogenesis and treatment strategies, thereby advancing the field.

6. Conclusion

Propionibacterium acnes plays a critical role in acne pathogenesis, triggering inflammatory and immune responses through multiple pathways, ultimately leading to acne onset and progression. Although significant progress has been made in understanding the pathogenic mechanisms of P. acnes, many unresolved challenges remain. Future research should prioritize genomics studies on P. acnes, investigations into host-microbe interaction mechanisms, and the development of novel therapeutic approaches. These efforts aim to provide more effective strategies for acne prevention and treatment. Through continuous research and exploration, we hope to achieve better treatment outcomes and improve the quality of life for acne patients.

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