Immunology: Current Research

mini review Open Access

Complement System: Immunity, Disease, And Therapeutics

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Received: 01-Jul-2025, Manuscript No. icr-25; **Editor assigned:** 03-Jul-2025, PreQC No. icr-25(PQ); **Reviewed:** 17-Jul-2025, QC No. icr-25; **Revised:** 22-Jul-2025, Manuscript No. icr-25(R); **Published:** 29-Jul-2025, **DOI**: 10.4172/icr.1000271

Citation: Novak DT (2025) Complement System: Immunity, Disease, And Therapeutics. Immunol Curr Res 09: 271.

Abstract

The complement system is a vital component of innate immunity, involved in pathogen defense and immune complex clearance. Its dysregulation is implicated in inflammatory and autoimmune diseases. This review explores key complement pathways, including lectin, alternative, and terminal pathways, and their therapeutic implications. Anaphylatoxins, complement regulators, and cross-talk with other immune systems are discussed. Emerging roles in neuroinflammation, cancer immunity, and as diagnostic markers are highlighted, alongside therapeutic strategies targeting the complement cascade.

Keywords

Complement System; Innate Immunity; Inflammatory Diseases; Autoimmune Diseases; Therapeutic Targets; Lectin Pathway; Alternative Pathway; Terminal Pathway; Anaphylatoxins; Complement Regulation

Introduction

The complement system stands as a cornerstone of innate immunity, providing an immediate defense against invading pathogens and playing a vital role in the clearance of immune complexes. Its intricate involvement in both health and disease states, particularly inflammatory and autoimmune conditions, underscores its complex and multifaceted nature. Recent research has shed light on novel regulatory mechanisms and identified potential therapeutic targets within the complement cascade, opening new avenues for intervention [1].

Understanding the delicate equilibrium of complement activation and regulation is paramount for the development of precise and effective therapeutic strategies. Emerging research is actively exploring the roles of specific complement proteins and their inhibitors in a range of diseases, including age-related macular degeneration and lupus nephritis, paving the way for personalized treatment approaches [2].

The lectin pathway, initiated through carbohydrate recognition domains, is a significant component of host defense against a wide array of pathogens. Contemporary studies have elucidated the structural and functional interdependencies of lectin pathway components, offering profound insights into its contribution to robust immune responses [3].

Complement anaphylatoxins, such as C3a and C5a, are potent initiators of inflammation and are critical for the recruitment of immune cells to sites of infection or injury. The receptors and signaling pathways associated with these molecules are increasingly recognized as important targets for modulating inflammatory diseases, with emerging evidence pointing to their involvement in neuroinflammation and cancer immunity [4].

The terminal complement pathway, culminating in the formation of the membrane attack complex (MAC), is essential for the lysis of pathogens and compromised host cells. The development

of inhibitors targeting MAC formation is a growing area of research for diseases where complement-mediated lysis is particularly detrimental [5].

Effective regulation of the complement system is indispensable for preventing autoimmune reactions and self-attack. Deficiencies in complement regulatory proteins can precipitate severe autoimmune disorders, highlighting their crucial protective role. Ongoing research endeavors to precisely define the interactions between these regulators and complement components, as well as the mechanisms by which their dysfunction contributes to disease pathogenesis [6].

The alternative pathway serves as a potent amplification loop within the complement system and is critical for effective host defense. Dysregulation of this pathway is implicated in serious conditions such as paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome, prompting the development of targeted therapeutic strategies focused on its specific inhibition [7].

Products generated during complement activation can exert direct influences on cellular functions, including processes such as cell survival, proliferation, and migration. This understanding is fundamental to comprehending the behavior of immune cells in both healthy physiological states and various pathological conditions [8].

The intricate cross-talk between the complement system and other key immune pathways, including the coagulation cascade and the kallikrein-kinin system, is becoming increasingly recognized. This complex network of molecular interactions significantly contributes to the overall complexity and fine-tuning of inflammatory responses within the body [9].

Complement activation markers are emerging as valuable tools for the diagnosis and prognosis of a growing number of diseases. The measurement of specific complement components or their activation products holds promise for aiding in disease diagnosis, monitoring therapeutic responses, and predicting disease outcomes with greater accuracy [10].

Description

The complement system, a vital part of innate immunity, provides rapid defense against pathogens and assists in clearing immune complexes. Its dysregulation is linked to numerous inflammatory and autoimmune diseases, emphasizing its dual role in health and pathology. Current advancements are uncovering novel regulatory mechanisms and therapeutic targets within the complement cascade, offering new avenues for treatment [1].

A deep understanding of the complex balance between complement activation and its regulation is crucial for designing targeted therapies. New research is focusing on the involvement of specific complement proteins and inhibitors in conditions such as age-related macular degeneration and lupus nephritis, suggesting a future of personalized treatment strategies [2].

The lectin pathway, initiated by carbohydrate-binding domains, plays a significant role in protecting the host against a wide spectrum of pathogens. Recent studies have detailed the structural and functional relationships among lectin pathway components, providing valuable insights into its contribution to immune responses [3].

Complement anaphylatoxins, notably C3a and C5a, are potent mediators of inflammation and are key drivers of immune cell recruitment. Their receptors and signaling pathways are increasingly becoming central targets for managing inflammatory diseases, with emerging evidence supporting their involvement in neuroinflammation and cancer immunity [4].

The terminal complement pathway, responsible for generating the membrane attack complex (MAC), is critical for eliminating pathogens and target cells through lysis. Inhibitors of MAC formation are under development for various diseases where excessive complement-mediated lysis proves detrimental [5].

Proper regulation of the complement system is essential to prevent self-directed attacks. Deficiencies in complement regulatory proteins can result in severe autoimmune conditions, highlighting their importance in maintaining self-tolerance. Research continues to explore how these regulators interact with complement components and how their functional impairment contributes to disease development [6].

The alternative pathway of complement activation functions as a powerful amplification loop critical for host defense. Its aberrant activation is implicated in diseases like paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome, driving efforts to develop therapies that specifically inhibit this pathway [7].

Complement activation products have the capacity to directly influence various cellular functions, including cell survival, proliferation, and migration. This understanding is crucial for elucidating immune cell behavior in both normal physiological processes and pathological circumstances [8].

The intricate interplay between the complement system and other immune pathways, such as coagulation and the kallikrein-

kinin system, is gaining significant attention. This complex network of interactions contributes to the overall sophistication of inflammatory responses [9].

The utility of complement activation markers in the diagnosis and prognosis of various diseases is a rapidly evolving field. Measuring specific complement components or their activation products can significantly aid in disease identification, monitoring treatment efficacy, and predicting patient outcomes [10].

Conclusion

The complement system is a crucial part of the innate immune system, important for defense against pathogens and clearing immune complexes. Its dysregulation contributes to inflammatory and autoimmune diseases. Recent research focuses on understanding complement pathways, including the lectin, alternative, and terminal pathways, and their roles in various conditions. Anaphylatoxins like C3a and C5a are key inflammatory mediators. Complement regulators are essential for preventing self-attack, and their deficiencies can lead to autoimmune disorders. The interaction between complement and other systems like coagulation is also being studied. Therapeutic strategies are being developed to target specific complement components or pathways, and complement biomarkers are emerging for diagnosis and prognosis.

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