

Dysregulated Innate Immunity: Mechanisms and Implications for Disease

Introduction

The innate immune system serves as the body's first line of defense against pathogens, rapidly recognizing and responding to infectious and stress signals. Dysregulated innate immunity, however, occurs when these responses become excessive, prolonged, or misdirected, contributing to a wide array of diseases, including autoinflammatory disorders, chronic infections, and cancer. Understanding the mechanisms behind innate immune dysregulation is essential for developing targeted therapies that restore immune balance while preserving host defense.

Mechanisms of Dysregulation

Dysregulated innate immunity can arise from genetic mutations, epigenetic modifications, or environmental triggers. Key players include pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and cytosolic sensors like NOD-like receptors (NLRs), which detect pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). Aberrant activation of these pathways can lead to excessive cytokine production, inflammasome activation, and tissue damage.

Clinical Implications

Dysregulated innate immunity underlies numerous clinical conditions.

Autoinflammatory syndromes, such as familial Mediterranean fever and VEXAS syndrome, result from overactive innate signaling pathways. In chronic infections, impaired innate responses can fail to control pathogens, while in cancer, chronic inflammation mediated by innate immune cells can promote tumor growth and immune evasion.

Therapeutic strategies targeting dysregulated innate immunity include biologics that inhibit specific cytokines (e.g., IL-1, IL-6), small molecule inhibitors of inflammasomes, and modulators of PRR signaling. Personalized approaches based on molecular profiling of immune dysregulation are increasingly important for optimizing treatment and minimizing adverse effects.

Conclusion

Dysregulated innate immunity represents a critical factor in the pathogenesis of inflammatory, infectious, and neoplastic diseases. By elucidating the mechanisms that drive overactive or defective innate responses, researchers can develop targeted therapies that restore immune homeostasis. Advances in molecular diagnostics and immune profiling will continue to improve our understanding, paving the way for precision interventions that balance effective host defense with controlled inflammation.

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