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Role of Immunology in the Progression of Osteoarthritis

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Abstract

A comprehensive understanding of the molecular factors and regulatory mechanisms that contribute to osteoarthritis (OA) may establish innovative therapeutic strategies designed to influence the course of disease advancement. The prevailing conceptual framework surrounding OA is transitioning from a strictly mechanical ailment characterized by cartilage degradation to a multifaceted biological response interlinking biomechanics, inflammatory processes, and the immune system. Inflammatory mediators, encompassing cytokines including interleukin-1 and tumor necrosis factor α, pattern recognition receptors expressed on the surface such as toll-like receptors 2 and 4, complement components like C5, alongside pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs), activate the enzymatic cascade responsible for cartilage matrix degradation in OA. By redefining the joint as a unified organ, the interactions among the resident cells within the synovium, comprising macrophages and a range of immune cell types, seem to promote enzymatic activity in cartilage, which subsequently transmits signals back to the synovium, reinforcing a feed-forward loop of degradation. This review proposes to analyze the prospective roles of immune cells, like macrophages and T cells situated in the synovium, in the facilitation and modulation of the inflammatory response characteristic of OA.

Keywords: Cartilage; Immune cells; Macrophages; Macrophages; Osteoarthritis

Abbreviations

DAMPs: Damage-Associated Molecular Patterns; ICs: Immune Cells; IL-1β: Interleukin-1 β; MMPs: Matrix Metalloproteins; OA: Osteoarthritis; PAMPs: Pathogen-Associated Molecular Patterns; TNF-α: Tumor Necrosis Factor.

Introduction

Osteoarthritis (OA) is primarily thought to be a degenerative disorder of the articular cartilage, a growing amount of research indicates that all branches are involved with the immune system. When cartilage is initially injured due to genetic, metabolic, or mechanical reasons, many auto-antigens specific to that cartilage are released to activate the immune response. The complement system is triggered, immune cells (ICs) such as T cells, B cells, and macrophages invade the joint tissues, and cartilage-degrading substances like matrix metalloproteins (MMPs) and prostaglandin E2 are released, which further cause additional articular cartilage degradation [1]. The involvement of the complement system in the pathogenesis of OA leads to the inflammation of chondrocytes due to their major role in the activation of B-cells and T-cells. The inflammation-

induced synovium releases soluble substances, including chemokines and cytokines, which exacerbate osteoarthritis symptoms. The well-regulated equilibrium among both anabolic and catabolic mechanisms that preserve cartilage homeostasis gets disrupted in OA. This disruption is brought on by the production of several cytokines and the activation of inflammatory pathways. The two main pro-inflammatory cytokines that cause cartilage homeostasis to shift through increased catabolism and cartilage destruction are interleukin-1 β (IL-1β) and tumor necrosis factor (TNF-α) [2,3].

Role of Complement System in Osteoarthritis

The early defence mechanism of innate immunity is known as the complement system that initiates a systemic alarm reaction in response to challenges. The complement system can stimulate the acute phase response, draw phagocytic cells, promote vascular permeability, and activate B and T lymphocytes whenever it is active [4]. Three different mechanisms can activate the complement cascade. Complement components have been demonstrated to be synthesized by chondrocytes, and pro-inflammatory cytokines including IL-1β and TNF-α have been found to enhance synthesis in OA [5,6].

Role of Cytokines in OA

As the illness progresses, synovitis, or inflammation of the synovial membrane, is beginning to emerge as the primary characteristic of osteoarthritis. Further aggravation of OA symptoms is caused by several soluble substances, including chemokines and cytokines secreted by the inflammatory synovium [7]. The inflammation-inducing factors and release of chemicals during OA disrupt the typically controlled anabolic and catabolic process that maintains cartilage homeostasis with many cytokines. The two main pro-inflammatory cytokines that lead to the equilibrium of cartilage alteration in favour of increased cartilage breakdown and catabolism are IL-1β and TNF-α [8].

Role of Macrophages in OA

The predominant cells in the OA synovium are macrophages, which produce cytokines that promote inflammation, like IL-1β and TNF-α, that are correlated with cartilage degradation. Activated macrophages can create possibilities for activated macrophages to manifest the reaction to endogenous DAMPS and PAMPs. Innate immune receptors called pattern recognition receptors are germline-encoded and capable of identifying both endogenous DAMPs and exogenous PAMPS [9]. According to recent studies, basic calcium phosphate crystal trigger PI3K, MAPK, and Syk provoking human macrophages to produce the DAMP antigen S100A8, IL-1β, and MMP1. The results indicate that manage with Syk inhibitors, some of them are presently undergoing clinical trials for autoimmune diseases and cancer, can help to reduce inflammation and cartilage damage caused by DAMP and crystals. Syk inhibition significantly reduced these cellular reactions [10,11].

Role of T cell in OA

Though its pathogenic significance in OA remains unknown, a substantial body of research suggests that OA synovium is having higher concentration of T lymphocytes than does healthy synovium [12]. A review was recently conducted on the function of effector T-cells, including as Th22, Th17, Th9, Th2, and Th1, in OA. RA synovium has considerably more common pro-inflammatory Th1 cells than OA synovial membranes, despite the latter's production of TNF-α and IFN-γ by subliming layer synovial membranes [13].

Role of other immune cells in OA

Plasma cells, mast cells and B-cells, are among the additional ICs found in OA synovial tissue [14]. There don't seem enough research, though, to demonstrate a link between B cell infiltration and the severity or course of OA. Mast cells were shown to be much more prevalent in OA samples and there was a positive correlation among the quantity of mast cells. Although mast cell degranulation can be induced by mechanical loading, a minority of OA samples (7%) have activated mast cells, as shown by substance P. Confirmation of potential pathogenic involvement of B cells or mast cells in the development of OA requires more research [15].

Conclusion

Recent research efforts have revealed important mechanistic perspectives on the roles of inflammation and immune cells in the pathophysiological landscape of OA. The development of OA evidently demands the activation of the complement system and the infiltration of macrophages. Subsequent investigative pursuits centered on assessing the localized suppression of complement activation or the deterrence of macrophage infiltration during the pivotal post-injury phase are critical to determine whether addressing these parameters may alleviate the progression towards end-stage OA. The observation of activated macrophages and T cell infiltration within the synovial fluid signifies predictors of pain and the progression of osteoarthritis; however, more extensive research is required to uncover the mechanisms through which this enduring low-grade inflammation contributes to the impairment of cartilage integrity.

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