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Beyond the Cells: Advancing Cartilage Tissue Engineering through Integrated Therapies

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Articular cartilage injuries remain a significant clinical challenge due to the tissue inherently limited capacity for self-repair. However, recent advancements in tissue engineering have introduced regenerative strategies aimed at restoring cartilage function. This systematic review consolidates current evidence from studies employing combinations of cellular therapies, biomaterial scaffolds, biochemical strategy, mechanical stimulation and translational approaches to enhance cartilage regeneration. The search was conducted in accordance with PRISMA guideline through a comprehensive literature search across PubMed, Scopus and Web of Science targeting peer-reviewed studies published between 2014 and 2024. Eligible studies focused on cartilage tissue engineering strategies involving therapeutic cells, biomaterials, biochemical or mechanical stimuli, and either preclinical or clinical applications. Following independent data extraction and classification by multiple reviewers, studies were grouped into five main themes: cell sources, biomaterial scaffolds, biochemical cues, mechanical/biophysical stimulation, and translational applications. Among cellular strategies, epiphyseal chondroprogenitor cells (ECPs), mesenchymal stromal cells (MSCs) and human mesenchymal stem cells (hMSCs) were frequently studied, each demonstrating varying degrees of chondrogenic potential. Concurrently, biomaterial scaffolds such as hydrogels, 3D-printed structures and ECM-derived matrices were shown to support chondrogenesis by mimicking the native extracellular matrix (ECM). Moreover, growth factors like TGF-β, IGF-I and novel peptides such as TP8 enhanced chondrocyte activity and ECM synthesis. These were often delivered via advanced, controlled-release systems. In conclusion, synergistic use of cell-based therapies, biomaterials, and bioactive signals may significantly enhance the outcomes of cartilage regeneration.

Keywords: Biomaterial Scaffolds, Cartilage Regeneration, Chondrogenic, Tissue Engineering, Mesenchymal Stem Cells (MSCs)

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