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WHERE ARE WE FAILING IN CARTILAGE REGENERATION? – A BATTLE OF TREATMENT HYPOTHESES

ICRS/ON RESEARCH FELLOWS ADVANCING ORTHOREGENERATION

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Purpose: Despite extensive research, no surgical, material, cell- or drug-based treatment reliably restores the structure and function of hyaline cartilage. This is partly because we do not fully understand why articular cartilage fails to regenerate. This review offers a synoptic and structured analysis of the field to guide the development of next-generation therapies for cartilage repair.

Methods and Materials: Current possible hypotheses to support why cartilage fails to regenerate were reviewed by the authors alongside the potential therapeutic strategies that are currently under investigation or in clinical use. Although this review aimed to target the repair of cartilage defects, some approaches described as current or potential therapies for osteoarthritis were included, due to the overlap of the underlying biological or mechanical processes in their pathophysiology.

Results: Five hypotheses were identified. The first hypothesis describes the lack of cells capable of regeneration in cartilage. Cell therapies address this by delivering or recruiting de-differentiated cells within the injured joint. Mechanical failure was the second hypothesis; addressed clinically by realignment and by joint distraction. Inflammatory stress was the third hypothesis, which is targeted with pharmaceuticals. In recent years, gene and cellular therapy strategies have advanced in this field, although further research is required. The final hypothesis was metabolic stress. Novel therapies to modulate mitochondrial homeostasis and antioxidant properties of chondrocytes are emerging, with mixed results currently.

Conclusion: This review highlighted the multiple hypotheses underlying the lack of cartilage regeneration, and devised the chronology of contribution of the individual hypotheses into a vicious cycle that leads to total joint damage. It also suggested the necessary checkpoints required to develop an effective regenerative treatment. Many promising new treatments are emerging, but none have led to major breakthroughs in cartilage regeneration. Future trials should aim to increase our understanding of cartilage's pathophysiology in addition to improving symptoms.

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