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Enhancement of Rotator Cuff Regeneration via Injectable Spheroidal Adipose-derived Stem Cell Cluster-Collagen Hydrogel Complex

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Introduction and Background

Rotator cuff repair frequently results in scar formation rather than true tendon regeneration, contributing to reduced mechanical strength and high re-tear rates. This study aimed to evaluate the regenerative efficacy and safety of an injectable complex composed of adipose-derived stem cell (ADSC) spheroids combined with collagen in an animal model of rotator cuff injury.

Material and Method

Human ADSCs were formed into spheroids and incorporated into a collagen matrix. Rats with surgically induced supraspinatus injury were assigned to four groups: (1) untreated control, (2) ADSC spheroids only, (3) collagen only, and (4) ADSC spheroid–collagen combination. Tendon healing was assessed using histology (H&E, Masson's trichrome, Safranin O, and picrosirius red) and biomechanical testing. Safety was evaluated through biodistribution, toxicity, and tumourigenicity assessments in immunosuppressed mice.

Results

Gene expression analysis showed that the ADSC spheroid–collagen complex upregulated regeneration-related transcription factors, supporting its tenogenic potential. Histological evaluation demonstrated significantly higher scores in the combination group compared with control (11.33 ± 0.61 vs. 8.33 ± 1.33, $p = 0.001$). Biomechanical testing showed improved failure load in the combination group (16.57 ± 4.58 vs. 7.94 ± 1.44 N, $p = 0.005$). Biodistribution analysis revealed no migration of administered cells to other organs, and no systemic toxicity or tumourigenesis was observed. Notably, transplanted cells remained localized at the injection site for up to 16 weeks.

Conclusions

The injectable ADSC spheroid–collagen complex significantly enhanced tendon regeneration and biomechanical strength in a rotator cuff injury model while demonstrating a favorable safety profile. The sustained local persistence and regenerative efficacy of this formulation indicate its strong potential as a clinically applicable cell-based therapeutic strategy for rotator cuff repair.