Adhesive Injectable Hydrogel-Loaded Exosomes for Advancing Osteoarthritis Therapy

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INTRODUCTION: Osteoarthritis (OA) poses a significant health burden with wide-reaching socioeconomic implications. Mesenchymal stem cell-derived exosomes (MSC-exosomes) hold promise for OA treatment, yet their swift clearance in vivo hampers therapeutic effectiveness. Thus, innovative strategies are needed to ensure efficient delivery and prolonged presence of exosomes at the injury site to optimize therapeutic outcomes.

METHODS: We developed an adhesive injectable hydrogel (aiGel) as a delivery platform for mesenchymal stem cell-derived exosomes (MSC-exosomes) to target and enhance their reparative potential in osteochondral defect regions. The destabilization of the medial meniscus (DMM) surgery was employed to create an osteoarthritis (OA) model in mice, followed by intra-articular injections of treatments one-month post-DMM surgery.

RESULTS SECTION: After treatment for one month, co-administration of MSC-exosomes with aiGel notably enhanced their retention within the joint cavity compared to MSC-exosomes alone. Co-treatment improved therapeutic efficacy by reducing cartilage destruction and promoting cartilage extracellular matrix regeneration. Remarkably, the combined therapy effectively alleviated pain associated with osteoarthritis in DMM mice, evidencing by gait analysis.

DISCUSSION: The adhesive injectable hydrogel (aiGel) allows for controlled exosome release. Further investigations are warranted to optimize dosage parameters, such as the minimal effective dose and maximal efficacy.

SIGNIFICANCE/CLINICAL RELEVANCE:
aiGel provides a vehicle for efficient delivery and sustained release of therapeutic exosomes into the synovial cavity, presenting a promising avenue for treating OA. This combination approach opens new prospects for advancing OA treatment strategies.

REFERENCES: NA

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IMAGES AND TABLES:

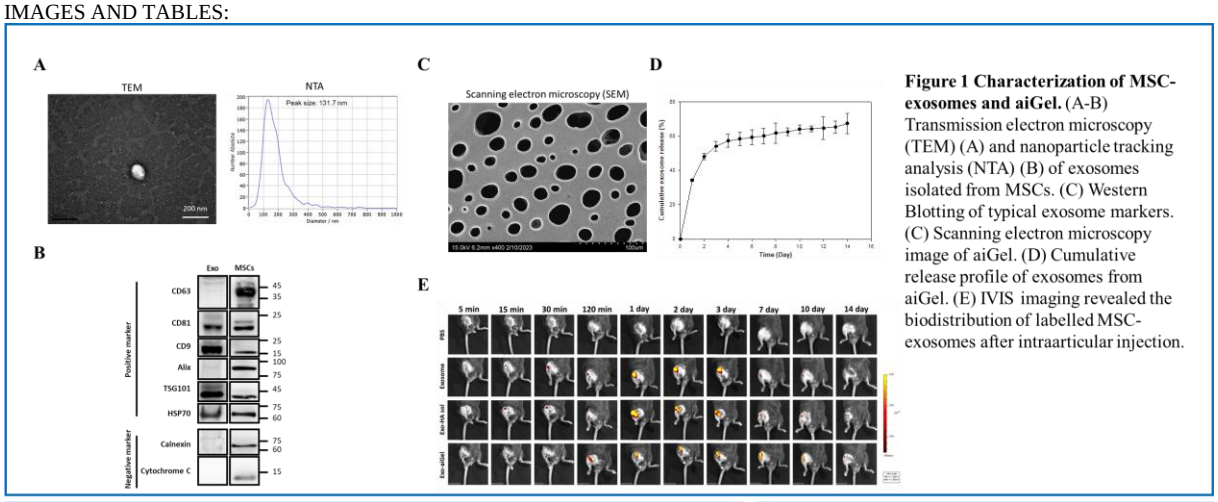

Figure 1 Characterization of MSC-exosomes and aiGel. (A-B) Transmission electron microscopy (TEM) (A) and nanoparticle tracking analysis (NTA) (B) of exosomes isolated from MSCs. (C) Western Blotting of typical exosome markers. (C) Scanning electron microscopy image of aiGel. (D) Cumulative release profile of exosomes from aiGel. (E) IVIS imaging revealed the biodistribution of labelled MSC-exosomes after intraarticular injection.

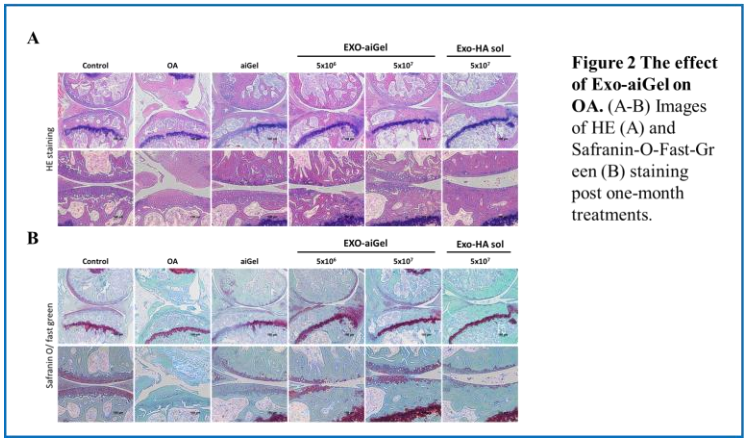

Figure 2 The effect of Exo-aiGel on OA. (A-B) Images of HE (A) and Safranin-O-Fast-Green (B) staining post one-month treatments.

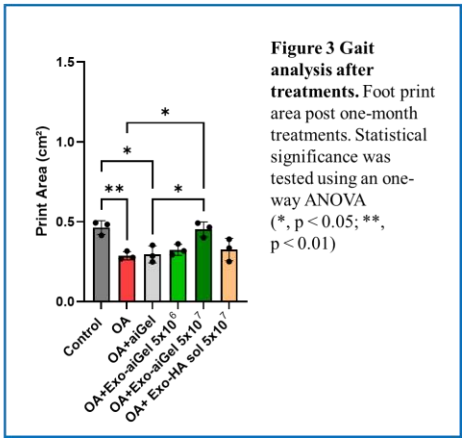

Figure 3 Gait analysis after treatments. Foot print area post one-month treatments. Statistical significance was tested using an one-way ANOVA (*, $p < 0.05$; **, $p < 0.01$)