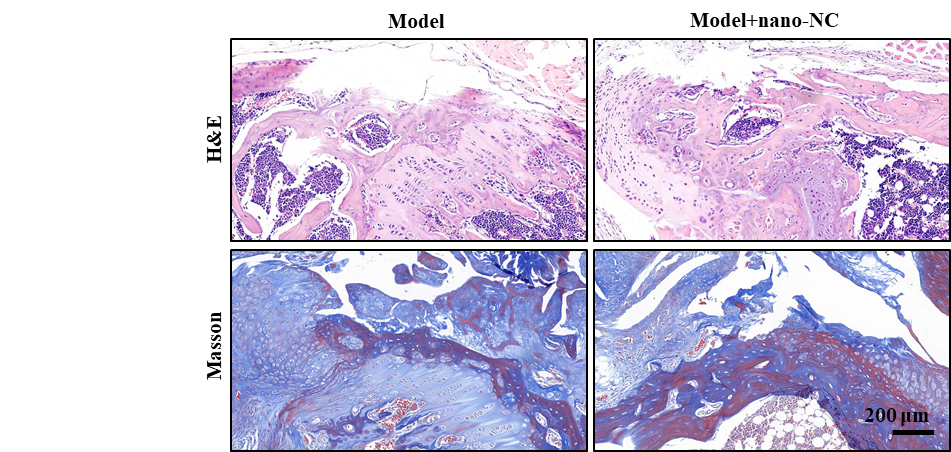
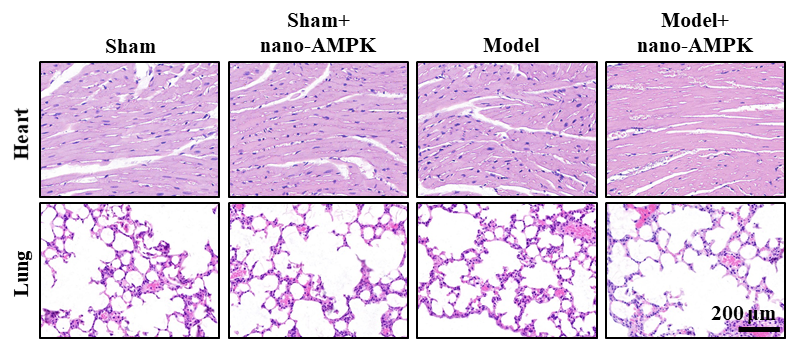
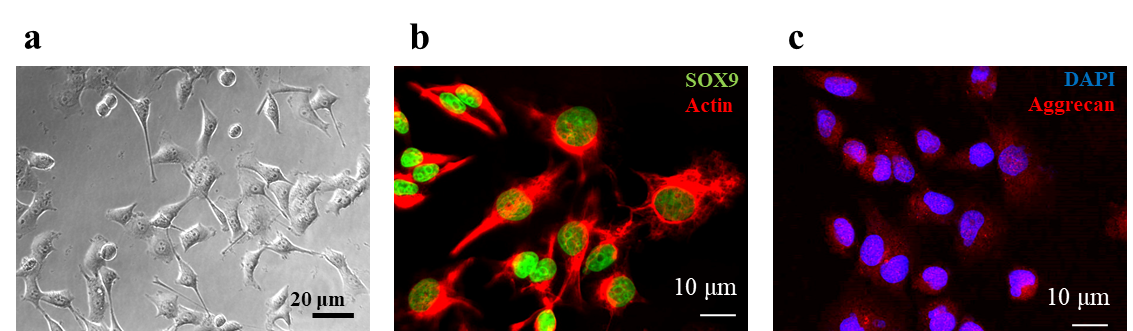
**Supplementary Materials**

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**Fig. S1. The nanocarrier alone showed no therapeutic effect on cartilage in experimental osteoarthritis rats.** Administration of nanocarrier without AMPK demonstrated no protective effects on articular cartilage, indicating that the therapeutic benefits observed in the main study were specifically attributed to the nano-AMPK rather than the delivery system itself.



**Fig. S2. Histological evaluation of heart and lung tissues after treatment.** H&E staining of heart and lung tissues from rats in different treatment groups showed no histopathological abnormalities. The normal tissue architecture was preserved in all treatment groups, demonstrating the safety of the administered treatments with respect to these vital organs.



**Fig. S3. Characterization of isolated primary chondrocytes.** (a) Phase-contrast microscopy images showing typical polygonal morphology of chondrocytes at different passages. The isolated cells maintained their characteristic chondrocyte morphology in early passages, displaying polygonal shapes with appropriate size distribution. (b-c) Immunofluorescence staining of chondrocyte-specific markers including SOX9 (key chondrocyte-specific transcription factor), and aggrecan (essential cartilage matrix protein) confirmed the identity and purity of the isolated chondrocytes.