A study led by Prof. Qiuyu Zhang (Northwestern Polytechnical University), Prof. Ki-Bum Lee (Rutgers University), and Prof. Liang Kong (School of Stomatology, The Fourth Military Medical University) has established an injectable hybrid inorganic (IHI) nanoscaffold-templated stem cell assembly system for advanced 3D stem cell culture and implantation. 3D-IHI nanoscaffold rapidly assembles stem cells into injectable tissue constructs through tailored 3D cell-cell and cell-matrix interactions, deeply and homogeneously delivers chondrogenic proteins in the assembled 3D culture systems, and controllably induces chondrogenesis through nanotopographical effects.

Once implanted in vivo in a rabbit cartilage injury model, 3D-IHI nanoscaffold effectively modulates dynamic microenvironment after cartilage injury through the integration of the aforementioned regenerative cues, and simultaneously scavenges reactive oxygen species using a manganese dioxide-based composition. In this way, accelerated repair of cartilage defects with rapid tissue reconstruction and functional recovery is realized both in the short term and long term. Given the excellent versatility and therapeutic outcome of 3D-IHI nanoscaffold-based cartilage regeneration, it may provide promising means to advance a variety of tissue engineering applications.
The research was published in *National Science Review.*

(a) A schematic diagram showing the 3D-IHI nanoscaffold could enhance chondrogenic differentiation of BMSC through a synergy between N-cadherin and FAK-mediated pathways. b) The strong interactions between MnO$_2$ NTs and functional groups commonly existing in ECM proteins effectively supported cell attachment as demonstrated via SEM image. c) Biochinnonic acid assay indicated the enhanced absorption toward gelatin from MnO$_2$ nanotube compared to control groups. d) The MnO$_2$ nanotube-templated assembly method significantly enhanced cell-matrix interaction as demonstrated through the up-regulated expression patterns of the FAK gene. e) Representative immunostaining images showing the improved chondrogenesis of BMSC in the BMSC-IHI nanoscaffold group compared to the control groups. Scale bar: 50 μm. f-h) The expression of chondrogenic genes, including SOX9 (f), Aggrecan (g), and Col-II (h) were characterized via qRT-PCR measurement. Credit: Science China Press
a) A schematic diagram illustrating the long-term (3 months) cartilage regeneration process. 
b) The in vivo cartilage regeneration was characterized through H&E, Safranin O staining, Col-II immunohistochemistry staining, as well as macroscopic views. Zoom out scale bar: 2 mm, zoom in scale bar: 200 μm. 
c-h) Quantifications of cartilage thickness (by H&E staining) (c), cellular components (by Safranin O staining) (d), ECM components (by Col II immunostaining) (e). Results of International Cartilage Repair Society (ICRS) macroscopic (f) and histologic scores (g) indicated significantly improved defect repair qualities in the TGF-β-BMSC-IHI nanoscaffold group. The reduced Osteoarthritis Research Society International (OARSI) scores revealed the TGF-β-BMSC-IHI nanoscaffold could prevent the deterioration of osteoarthritis (h). Credit: Science China Press


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