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## ACCEPTED MANUSCRIPT

### Carbohydrate Polymers

# The three dimensional cues-integrated-biomaterial potentiates differentiation of human mesenchymal stem cells

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### Highlights

- A novel biochemical and biophysical cues-integrated-biomaterial (CiB) platform is reported.
- CiB is composed of cells derived extracellular matrix (FDM) and alginate hydrogels.
- CiB mimics stem cells microenvironment, enhances cells viability and proliferation.
- CiB offers easy to fabricate 3D cell culture system.
- CiB induces specific chondrogenic and osteogenic differentiation of stem cells.

#### Abstract

Alginate (Alg) hydrogels, the most popular natural biomaterials, mimic extracellular matrix (ECM) microenvironment and offer potential biomedical applications. Despite their excellent properties such as biocompatibility, hydrophilicity and ionic crosslinking, the absence of an intrinsic cell adhesion domain lessens their cell-carrier applications in tissue engineering. Herein, we suggest a three-dimensional (3D) cell culture system by integrating Alg hydrogel and fibroblast-derived matrix (FDM). FDM including cell-adhesion motifs, signaling, and physico-mechanical cues is prepared by the decellularization process by avoiding unfavorable chemical reactions. This cues-integrated-biomaterials (CiB) 3D platform shows increased cell viability, proliferation, chondrogenic and osteogenic differentiation of human bone-marrow-derived mesenchymal stem

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