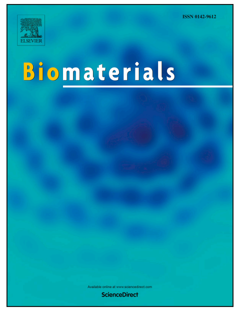
Accepted Manuscript



Stiffness memory of indirectly 3D-printed elastomer nanohybrid regulates chondrogenesis and osteogenesis of human mesenchymal stem cells

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PII: S0142-9612(18)30644-6

DOI: 10.1016/j.biomaterials.2018.09.013

Reference: JBMT 18884

To appear in: *Biomaterials*

Received Date: 21 June 2018

Revised Date: 28 August 2018

Accepted Date: 8 September 2018

Please cite this article as: Wu L, Magaz Adriá, Wang T, Liu C, Darbyshire A, Loizidou M, Emberton M, Birchall M, Song W, Stiffness memory of indirectly 3D-printed elastomer nanohybrid regulates chondrogenesis and osteogenesis of human mesenchymal stem cells, *Biomaterials* (2018), doi: 10.1016/j.biomaterials.2018.09.013.

Stiffness memory of indirectly 3D-printed elastomer nanohybrid regulates chondrogenesis and osteogenesis of human mesenchymal stem cells

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Abstract: The cellular microenvironment is dynamic, remodeling tissues lifelong. The biomechanical properties of the extracellular matrix (ECM) influence the function and differentiation of stem cells. While conventional artificial matrices or scaffolds for tissue engineering are primarily static models presenting well-defined stiffness, they lack the responsive changes required in dynamic physiological settings. Engineering scaffolds with varying elastic moduli is possible, but often lead to stiffening and chemical crosslinking of molecular structure with limited control over scaffold architecture. A family of indirectly 3D printed elastomeric nanohybrid scaffolds with thermoresponsive mechanical properties that soften by inverse self-assembling at body temperature have been developed recently. The initial stiffness and subsequent stiffness relaxation of the scaffolds regulated the proliferation and differentiation of human bone-marrow derived mesenchymal stem cells (hBM-MSCs) towards the chondrogenic and osteogenic lineages over 4 weeks, as measured by immunohistochemistry, histology, ELISA and qPCR. hBM-MSCs showed enhanced chondrogenic differentiation on softer scaffolds and osteogenic differentiation on stiffer ones, with similar relative expression to that of human femoral head tissue. Overall, stiffness relaxation favored osteogenic activity over chondrogenesis *in vitro***.**

Keywords
Stiffness memory, stem cell differentiation, chondrogenesis, osteogenesis, 3D printing, elastomer nanohybrid