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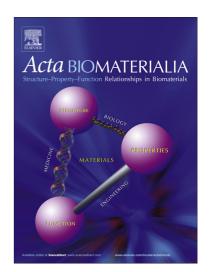
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## **ACCEPTED MANUSCRIPT**

Differentiation of mesenchymal stem cells for cartilage tissue engineering: Individual and synergetic effects of three-dimensional environment and mechanical loading

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#### **Abstract**

Chondrogenesis of dedifferentiated chondrocytes and mesenchymal stem cells is influenced not only by soluble molecules like growth factors, but also by the cell environment itself. The latter is achieved both through mechanical cues – which act as stimulation factor and influences nutrient transport - and through adhesion to extracellular matrix cues – which determine cell shape. Although the effects of soluble molecules and cell environment have been intensively addressed, few observation and conclusions about the interaction between both of them have been achieved. In this work, we review the state of the art on the single effects between mechanical and biochemical cues, as well as on the combination of both. Furthermore, we provide a discussion on the techniques currently used to determine the mechanical properties of materials and tissues generated in vitro, their limitations and the future research needs to properly address the identified problems.

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