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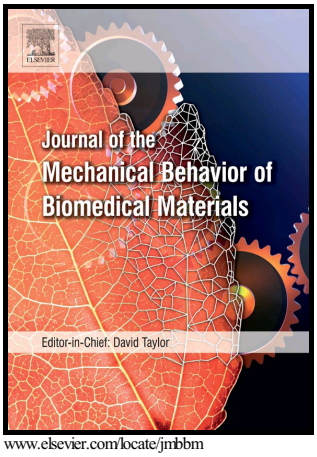

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Matrix architecture plays a pivotal role in 3D osteoblast migration: the effect of interstitial fluid flow

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Abstract

Osteoblast migration is a crucial process in bone regeneration, which is strongly regulated by interstitial fluid flow. However, the exact role that such flow exerts on osteoblast migration is still unclear. To deepen the understanding of this phenomenon, we cultured human osteoblasts on 3D microfluidic devices under different fluid flow regimes. Our results show that a slow fluid flow rate by itself is not able to alter the 3D migratory patterns of osteoblasts in collagen-based gels but that at higher fluid flow rates (increased flow velocity) may indirectly influence cell movement by altering the collagen microstructure. In fact, we observed that high fluid flow rates (1 µl/min) are able to alter the collagen matrix architecture and to indirectly modulate the migration pattern. However, when these collagen scaffolds were crosslinked with a chemical crosslinker, specifically, transglutaminase II, we did not find significant alterations in the scaffold architecture or in osteoblast movement. Therefore, our data suggest that high interstitial fluid flow rates can regulate osteoblast migration by means of modifying the orientation of collagen fibers. Together, these results highlight the crucial role of the matrix architecture in 3D osteoblast migration. In addition, we show that interstitial fluid flow in conjunction with the matrix architecture regulates the osteoblast morphology in 3D.

Competing Interests: A provisional Spanish patent application that covers the support for the fluid flow application disclosed in this manuscript has been submitted. CDA, AB, JS, and JMGA are listed as inventors on this application.

Keywords: osteoblast migration, transglutaminase, interstitial fluid flow, fibers, collagen-based matrices, crosslinkers

1. Introduction