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BIOMIMETIC BIOREACTORS AS A TOOL FOR MORE RELEVANT BIOMATERIAL ASSESSMENT

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Abstract

Development of novel biomaterials for use in biomedical applications requires careful assessment due to the intended interactions with cells and tissues. Understanding biocompatibility, non-toxicity, and capability of promoting desired biological responses requires thorough characterization of biomaterial, including its chemical composition, surface properties, mechanical strength, degradation rate, etc. Traditional *in vitro* methods for evaluating biomaterials in cell monolayers are convenient but limited by the lack of specific biophysical signals found *in vivo*, which can lead to unreliable results. This *in vitro-in vivo* gap can result in the unnecessary sacrifice of a large number of animals for testing purposes. Therefore, there is a need for alternative approaches that better mimic the *in vivo* environment and accurately predict the behavior of the biomaterial after implantation. Biomimetic bioreactors are primarily developed for tissue engineering to provide the key biochemical (e.g., nutrients, gases, growth factors) and biophysical signals (e.g., shear stress, hydrostatic pressure, mechanical strains) found *in vivo* and thus could be indispensable tools in physiologically relevant biomaterial assessment. Our group introduced the application of two biomimetic bioreactors for the physiologically relevant characterization of two types of composite biomaterials aimed for bone and osteochondral tissue engineering. In specific, macroporous composite scaffolds were produced using two natural polymers (gellan gum and alginate) as matrices imitating organic phase of bone tissue with incorporated particulate bioactive glass (BAG) and β-tricalcium phosphate (β-TCP) as hydroxyapatite (HAp) precursors. In addition, in osteochondral scaffolds, gellan gum hydrogel served as a cartilaginous layer on top of the porous composite base. Integrity and mechanical properties of all prepared scaffolds were monitored for 14 days under physiological levels of mechanical compression (up to 10% strain, compression rate 337.5 µm s-1) in a bioreactor with dynamic compression and medium perfusion. Bioactivity and HAp formation within the scaffolds were investigated in a perfusion bioreactor under the flow of simulated body fluid for up to 28 days. The scaffolds were assessed by SEM, EDS, and XRD analyses indicating a significant increase in HAp formation under bioreactor conditions as compared to static controls in all investigated samples. Moreover, the formed HAp crystals were more uniformly distributed throughout the scaffolds showing a more cauliflower-like morphology and thus, indicating potentials for bone/osteochondral tissue engineering applications. The obtained results confirm the high influence of experimental conditions on the outcomes of biomaterial characterization and importance of closely mimicking physiological conditions, thus putting forward biomimetic bioreactors as a means in this direction.