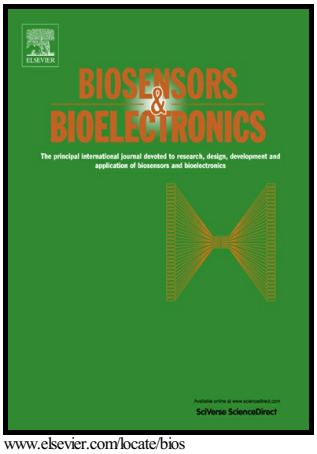

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Sensing Metabolites for the Monitoring of Tissue Engineered Construct Cellularity in Perfusion Bioreactors

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Abstract

As the field of tissue engineering progresses ever-further toward realizing clinical implementation of tissue-engineered constructs for wound regeneration, perhaps the most significant hurdle remains the establishment of non-destructive means for real-time *in vitro* assessment. In order to address this barrier, the study presented herein established the viability of the development of correlations between metabolic rates (specifically oxygen uptake, glucose consumption, and lactate production) and the cellularity of tissue-engineered cultures comprised of rat mesenchymal stem cells dynamically seeded on 85% porous nonwoven spunbonded poly(L-lactic acid) fiber mesh scaffolds. Said scaffolds were cultured for up to 21 days in a flow perfusion bioreactor system wherein α-MEM (supplemented with 10% fetal bovine serum and 1% antibiotic-antimycotic) was perfused directly through each scaffold at low flow rates (~0.15 mL/min). Metabolite measurements were obtained intermittently through the use of a fiber-optic probe (for the case of oxygen) and biochemical assays (for glucose and lactate). Such measurements were subsequently correlated with cellularity data obtained utilizing current-standard destructive means. The resulting correlations, all exhibiting high R^2 values, serve as a proof-on-concept for the use of metabolic data for the determination of scaffold cellularity in real-time non-destructively. This study can be easily adapted for use with various cell types, media formulations, and potentially different bioreactor systems. Implementation of more