World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:9, No:04, 2015

Study of the Combinatorial Impact of Substrate Properties on Mesenchymal Stem Cell Migration Using Microfluidics

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Abstract : Cell Migration is a vital phenomenon that the cells undergo in various physiological processes like wound healing, disease progression, embryogenesis, etc. Cell migration depends primarily on the chemical and physical cues available in the cellular environment. The chemical cue involves the chemokines secreted and gradients generated in the environment while physical cues indicate the impact of matrix properties like nanotopography and stiffness on the cells. Mesenchymal Stem Cells (MSCs) have been shown to have a role wound healing in vivo and its migration to the site of the wound has been shown to have a therapeutic effect. In the field of stem cell based tissue regeneration of bones and cartilage, one approach has been to introduce scaffold laden with MSCs into the site of injury to enable tissue regeneration. In this work, we have studied the combinatorial impact of the substrate physical properties on MSC migration. A microfluidic in vitro model was created to perform the migration studies. The microfluidic model used is a three compartment device consisting of two cell seeding compartments and one migration compartment. Four different PDMS substrates with varying substrate roughness, stiffness and hydrophobicity were created. Its surface roughness and stiffness was measured using Atomic Force Microscopy (AFM) while its hydrphobicity was measured from the water contact angle using an optical tensiometer. These PDMS substrates are sealed to the microfluidic chip following which the MSCs are seeded and the cell migration is studied over the period of a week. Cell migration was quantified using fluorescence imaging of the cytoskeleton (F-actin) to find out the area covered by the cells inside the migration compartment. The impact of adhesion proteins on cell migration was also quantified using a real-time polymerase chain reaction (qRT PCR). These results suggested that the optimal substrate for cell migration would be one with an intermediate level of roughness, stiffness and hydrophobicity. A higher or lower value of these properties affected cell migration negatively. These observations have helped us in understanding that different substrate properties need to be considered in tandem, especially while designing scaffolds for tissue regeneration as cell migration is normally impacted by the combinatorial impact of the matrix. These observations may lead us to scaffold optimization in future tissue regeneration applications.

Keywords : cell migration, microfluidics, in vitro model, stem cell migration, scaffold, substrate properties
Conference Title : ICMBE 2015 : International Conference on Medical and Biomedical Engineering
Conference Location : Paris, France
Conference Dates : April 27-28, 2015