J Material Sci Eng 2016, 5:7 (Suppl)
http://dx.doi.org/10.4172/2169-0022.C1.047

6th International Conference and Exhibition on
Materials Science and Engineering
September 12-14, 2016 Atlanta, USA

Matrix resistance stress: A key parameter for immobilized cell growth regulation

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Irreversible nature of matrix structural changes around the immobilized cell aggregates caused by cell expansion is considered within the Ca-alginate microbeads. It is related to various effects: Cell-bulk surface effects (cell-polymer mechanical interactions) and cell surface-polymer surface effects (cell-polymer electrostatic interactions) at the bio-interface; polymer-bulk volume effects (polymer-polymer mechanical and electrostatic interactions) within the perturbed boundary layers around the cell aggregates; cumulative surface and volume effects within the parts of the microbead and; macroscopic effects within the microbead as a whole based on multi scale modeling approaches. Matrix irreversible structural changes within the boundary layers around the cell aggregates induces generation of the matrix resistance stress. The matrix stress is one of the key control parameters for the bioprocess optimization in order to achieve higher concentration of immobilized cells. The main rheological properties which gel matrix should satisfy are formulated in order to reduce the matrix resistance stress generated by compression within the boundary layers around the immobilized cell clusters caused by cell expansion. The stress reduction is prerequisite for achieving higher cell concentration within Ca-alginate beads. Two properties: the matrix viscoelasticity and the ability of stress relaxation have been proposed. In this work, we have connected these properties with loading conditions caused by cell rearrangement and growth occurred during repeated multi scale stress relaxation cycles. Herein, an attempt is made to discuss and connect various multi scale modeling approaches in order to shed further light to this complex course-consequence phenomenon.

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Thermo-responsible copolymer interaction with human induced pluripotent stem cells for functional and pyramidal neuron differentiation

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The interaction among human induced pluripotent stem cells (hiPSCs) with thermo-responsible copolymer substrates signifies to have a reflective impact on stem cells based applications in regenerative medicine and tissue engineering. Development and design of noval biomaterial that should be non-toxic and having unique properties that could drive stem cell fate both *in vivo* and *in vitro* is biggest challange. We report thermo-responsible solvent casting copolymer i.e. poly(N-isopropylacrylamide)(NiPAM)-co-poly(N-tert-butlyacrylamide) (NtBAM) system for guiding the hiPSCs more into pyramidal or cortical neurons fate. A three conditions (Control for iPSCs i.e. Geltrex; copolymer and Geltrex coated copolymer) was designed to carryout whole experiment using three iPSCs donors (1C-C1, 02V-C1 and 3V-C1). Presence of Geltrex, Copolymer and Geltrex coated copolymer were charachertized using Fourier transform infrared spectroscopy (FITR) and Scanning Electron Microscope (SEM). FTIR and SEM shows the presence of NIPAM, NtBAM and NIPAM-co-NtBAM on culture vessels. Atomic Force Microscope (AFM) was used to determine the roughness of Geltrex (48.13 nm), copolymer (33.07 nm) and blank (34.58 nm, without copolymer or Geltrex), respectively. Where thickness of Geltrex (338 nm) and copolymer (792.84 nm) were measured by AFM. An experiment for 15 days were designed for hiPSCs behaviour on three conditions. Geltrex cultured hiPSCs were in typical round, colony shaped till day 12 and found positive for pluripotent markers (OCT4, SOX2 and NANOG) with slightly differentiated cells; whereas hiPSCs on copolymer were change their morphological pattern from day one and differentiated into typical pyramidal neurons on day 12 and were positive with neuronal i.e. TUJ1, NESTIN, DCX, MAP2, ASM (Mesoderm) and AFP (Endoderm) markers using immunostaining, Western blot and qt-PCR methods. hiPSCs on Geltrex coated copolymer were in intermediated stage of iPSCs and neuronal differentiation. Hence, we conclude that there is strong correlation among laboratory designed copolymer and iPSCs differentiation into neuronal fate and NIPAM-co-NtBAM enchances the neuronal differentiation process i.e. neuronal stem cells, neuronal precursor cells or terminal differentiated neuronal cells. This specially designed copolymer system may pave a way for future rapid differentiation process and in the treatment of neuronal diseases.

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