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Nanowire Substrate to Control Differentiation of Mesenchymal Stem Cells

Authors : Ainur Sharip, Jose E. Perez, Nouf Alsharif, Aldo I. M. Bandeas, Enzo D. Fabrizio, Timothy Ravasi, Jasmeen S. Merzaban, Jürgen Kosel

Abstract : Bone marrow-derived human mesenchymal stem cells (MSCs) are attractive candidates for tissue engineering and regenerative medicine, due to their ability to differentiate into osteoblasts, chondrocytes or adipocytes. Differentiation is influenced by biochemical and biophysical stimuli provided by the microenvironment of the cell. Thus, altering the mechanical characteristics of a cell culture scaffold can directly influence a cell's microenvironment and lead to stem cell differentiation. Mesenchymal stem cells were cultured on densely packed, vertically aligned magnetic iron nanowires (NWs) and the effect of NWs on the cell cytoskeleton rearrangement and differentiation were studied. An electrochemical deposition method was employed to fabricate NWs into nanoporous alumina templates, followed by a partial release to reveal the NW array. This created a cell growth substrate with free-standing NWs. The Fe NWs possessed a length of 2-3 µm, with each NW having a diameter of 33 nm on average. Mechanical stimuli generated by the physical movement of these iron NWs, in response to a magnetic field, can stimulate osteogenic differentiation. Induction of osteogenesis was estimated using an osteogenic marker, osteopontin, and a reduction of stem cell markers, CD73 and CD105. MSCs were grown on the NWs, and fluorescent microscopy was employed to monitor the expression of markers. A magnetic field with an intensity of 250 mT and a frequency of 0.1 Hz was applied for 12 hours/day over a period of one week and two weeks. The magnetically activated substrate enhanced the osteogenic differentiation of the MSCs compared to the culture conditions without magnetic field. Quantification of the osteopontin signal revealed approximately a seven-fold increase in the expression of this protein after two weeks of culture. Immunostaining staining against CD73 and CD105 revealed the expression of antibodies at the earlier time point (two days) and a considerable reduction after one-week exposure to a magnetic field. Overall, these results demonstrate the application of a magnetic NW substrate in stimulating the osteogenic differentiation of MSCs. This method significantly decreases the time needed to induce osteogenic differentiation compared to commercial biochemical methods, such as osteogenic differentiation kits, that usually require more than two weeks. Contact-free stimulation of MSC differentiation using a magnetic field has potential uses in tissue engineering, regenerative medicine, and bone formation therapies.

Keywords : cell substrate, magnetic nanowire, mesenchymal stem cell, stem cell differentiation
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