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Stem cell developmental processes on biofunctional domains *in vitro*

Stem cells are characterized by two unique properties in one cell: their self-renewal capacity and their multilineage differentiation potential, which make them an ideal source for cellular therapy and regenerative medicine as well as for pharmaco-toxicological applications. However, to make such applications possible, the generation of appropriate stem cell models and the development of well-controlled procedures for in vitro stem cell expansion, differentiation and maintenance are required. Bioactive surface domains were applied to investigate cellular developmental processes of human cord blood- derived stem cells and to direct their fate into desired neural lineages. Such domains should represent microenvironmental cues resembling those found in vivo. For that purpose we have created miniaturized cell growth platforms with defined arrays of cell attractive biomaterials serving as functional domains. Emerging technologies applied included a nano/microfabrication technique like microcontact printing and piezoelectric (noncontact) microspotting of biomolecules on plasma deposited cell repellent surface. Human Umbilical Cord Blood Neural Stem Cell (HUCB-NSC) line was plated on biodomains at different concentrations and serum conditions. HUCB-NSCs were shown to adhere and differentiate on microarray platforms in a protein type, concentration and cell density dependent manner. Receptor-mediated interactions with extracellular proteins promote neuronal differentiation, while non-specific adhesion to polyaminoacid molecules allows maintaining of stem cells immobilized to the surface in non-differentiated stage. 'Smart' functional domains were created by immobilizing to the surface small signaling molecules (e.g wnt, shh, notch or jagged) together with ECM proteins. Stimulation of selected intracellular pathways by signaling molecules resulted in differentiation of HUCB-NSC to either neuronal or astroglial lineage. Miniaturization of such bioengineered active domains combined with appropriate stem cell model may allow application of such stem cell growth platforms for the multiparameter bio-tests and can provide important, additional information on the sensitivity of certain neural stem cell molecular pathways to the selected neurotoxins. Since HUCB-NSC can be cultured and harvested at different developmental stages and was shown to be a good model for developmental toxicity testing, homogeneous lineage related pluripotent population is required. For that purpose iPs cells from HUCB-NSC are produced.

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