Title: Retinoic Acid Receptor Overexpression in Human Umbilical Cord-derived Mesenchymal Stem Cells

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Abstract:
Introduction: Retinoic acid (RA) involves invertebrate morphogenesis, growth and apoptosis through two classes of receptors encoded by six genes: RAR(a, b, g) and RXR(a, b, g). The former utilizes either all-trans RA or 9-cis-RA as ligands, whereas the RXRs utilize only 9-cis-RA. Using the human umbilical cord derived stem cells (HUCSCs) as an in vitro model of human fetal cells we aimed to evaluate RAR overexpression following to RA treatment. Methods: Human umbilical matrix derived mesenchymal stem cells (HUCSCs) were cultured in DMEM + 10% FBS at a density of 1 × 10^3 well. Upon adhering, the medium was changed to DMEM containing RA for 4-6 days during which RA refreshed every 2 days. The cells cultured without RA were considered as a control group. Using a combination of flow cytometry, MTT colorimetric assay and conventional RT-PCR techniques, CD markers, cell viability and RAR expression profile of HUCSCs were measured, respectively. Results: Flow cytometry analysis clearly indicated 5.4% of HUCSCs co-expressed CD34 and CD45, while 63.7% of cells expressed both CD44 and CD73. 36.5% of cells expressed CD90 compared to 0.05% for CD105. MTT assay also showed that about 60% of HUCSCs viability decreased at higher doses (10^{-7}–10^{-5}) of RA compared to control group. RT-PCR analysis also revealed that RAR a and b were upregulated in the RA-treated cells. Conclusions: This study clearly shows that the HUCSCs express CD44, CD73 and CD90 and RA in a dose-dependent manner has cytotoxicity effect on HUCSCs that is mediated by RAR a and b.

Keywords: Human Umbilical Cord-derived mesenchymal Stem Cells, RAR, RXR, Retinoic acid, Cytotoxicity