OMICS Group Conferences
Accelerating Scientific Discovery

3rd World Congress on
Cell Science & Stem Cell Research
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, MD, USA

Alternative sources of mesenchymal stem cells for islet generation for diabetes research and therapeutics

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Bone marrow-derived mesenchymal stem cells (BMSCs) have been used for allogeneic application in tissue engineering but have certain drawbacks. Therefore, mesenchymal stromal cells (MSCs) derived from other postnatal tissue sources have been considered as an alternative. The human umbilical cord, amnion and placenta are easily available non-controversial tissue sources of human origin and their collection is non-invasive. These sources of MSCs are not subjected to ethical constraints, as in the case of embryonic stem cells. MSCs are multipotent stem cells and have the ability to differentiate into various cell types of the mesodermal lineage. The aim of this study was to establish a reproducible method for the isolation of MSCs from human umbilical cord, amnion, and placenta to compare their propensity towards pancreatic/islet lineage for utilization as a cell therapy product.

Experimental Design & Methods: Mesenchymal stromal cells (MSCs) were isolated from umbilical cord (UC MSC) amnion (AMSC) and, placenta (PMSCS) adipose tissue (AT) and dental pulp (DP) using different culture conditions with respect choice of medium and serum to optimize medium-scale production. On further expansion upto five passages, they were analyzed for surface as well as cytoskeletal markers. Their multilineage differentiation potential was tested by subjecting these to lineage specific differentiation cocktails.

Results: Extensive phenotypic characterization analysis of these cells, using flow cytometry and antibody staining methods, have shown that the MSCs expressed CD13, CD44, CD73, CD90, and CDIO5, but not CD31, CD34, CD45 and HLA-DR. These MSCs were also found to express vimentin, desmin and alpha-smooth muscle actin as cytoskeletal mesenchymal cell markers. When these MSCs were subjected to specific differentiation cocktails they could differentiate into adipogenic, chondrogenic, oesteogenic and islet lineage.

Conclusions: Mesenchymal stromal cells can be expanded from different sources of human origin retaining their multilineage differentiation potential *in vitro*. They represent a relatively homogeneous population of mesenchymal stromal cells. Our results indicate that fetal as well as postnatal tissues represent a rich source of mesenchymal stromal cells suitable for islet neogenesis *in vitro*. Therefore adipose tissue and dental pulp MSCs could be regarded as an alternative source of MSCs for experimental and clinical needs. Further studies are planned to examine their safety and efficacy in animal models of type1 and type 2 diabetes.

Biography

Ramesh Bhonde is a Professor and Dean, at the Manipal Institute of Regenerative Medicine, Bangalore. He superannuated from National Center for Cell Science Pune and joined Stempeutics Research Pvt. Ltd. He has been working in the field of pancreatic regeneration in diabetes for the past twenty years. He has extensively worked on in vitro generation of islets from pancreatic and non- pancreatic stem cells. He demonstrated that mesenchymal stem cells derived from human umbilical cord, placenta, amnion and adipose tissue are capable of differentiating into functional islets which could reverse experimental diabetes in mice upon transplantation. He has guided till now 18 Ph.D. students. He has more than 170 publications, of which 130 are listed in PubMed, 4 book chapters and 3 patents to his credit.

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