

Wharton's jelly mesenchymal stem cells differentiation into hepatocyte-like cells: functional characterization and expression of immunomodulatory molecules

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Mesenchymal stem cells derived from Wharton's jelly (WJ-MSCs) recently emerged as promising tools for cellular therapy due to their ability to differentiate into diverse cell types and their immunomodulatory features. Little is known on the expression of immunomodulatory molecules in mature cells differentiated from WJ-MSCs, therefore we aimed to characterize the extent of maintenance of the naive traits of these cells also in a highly specialized differentiated counterpart.

WJ-MSCs were differentiated into hepatocyte-like cells (HLCs) with a four weeks protocol. RT-PCR, flow cytometry, IHC and ICC were performed to assess expression of key markers in both undifferentiated and differentiated cells. Hepatocyte specific assays such as PAS staining, CYP3A4 induction and activity, G6Pase activity, were performed to demonstrate the acquisition of traits of the mature hepatocyte phenotype. WJ-MSCs were successfully differentiated into HLCs using a multi-step protocol. These cells were able to store glycogen, incorporate specific live cells stains, perform enzymatic reactions and metabolic activities which are usually featured by mature hepatocytes. In addition, WJ-MSCs did express several immune-related molecules, for which an immunomodulatory role has been demonstrated both in vitro and in vivo. We demonstrated for the first time that key molecules as HLA-E and B7-H3 are expressed also by HLCs derived from WJ-MSCs. Our data showed for the first time that HLCs mostly maintain the expression of immune-modulating molecules, together with new markers and functional features of mature cells. In multiple pathologic conditions the intrinsic immunomodulatory ability of differentiated cells may help survive the interaction with the host immune system, even in the absence of a specific immunosuppressive therapy. This, together with the acquisition of key mature hepatocyte functions, may render WJ-MSCs promising in cell therapy applications for liver diseases.

Keywords

Umbilical cord, perinatal stem cells, mesenchymal stem cells, hepatocyte differentiation, immune modulation.