POSTER ABSTRACTS

TSC148

ENHANCED IN VITRO HIPSC-DERIVED HEPATOCYTE-LIKE CELLS MATURATION

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The liver is a crucial organ regarding metabolic, immune and homeostatic regulation. Chronic and acute liver diseases, genetically determined or acquired, account for approximately 2 million deaths per year. The only therapeutic options to severe liver diseases are partial or total liver transplantation. Hepatic tissue engineering, combined with human induced pluripotent stem cells (hiPSCs) technology, offers an alternative to traditional therapeutic procedures. Hepatocytes differentiation protocols, nevertheless, result in hepatocytes with fetal phenotype, hampering the comprehension about adult liver cells mechanisms of regeneration, potential tissue engineering approaches, in vitro disease modeling and drug development applications. Here we show that the application of a formulation composed of cell death inducer molecules in hiPSC-derived hepatocytes (HLCs) for 24 h contributed for induction of hepatic maturation, which was confirmed through gene (RT-qPCR) and protein (immunofluorescence and flow cytometry) expression analyses. Mature hepatocyte differentiation markers, such as ALB, G6PC and TDO2, were overexpressed in the treated group, which also secreted significantly more albumin in culture. Finally, KRT7 and KRT19, hepatic biliary duct cells (i.e. cholangiocytes) related genes showed reduced expression. This new formulation may enhance current in vitro liver development assays, increase the accuracy of liver diseases modeling and of hepatotoxicity assays and improve current stem cell-based bio-artificial liver engineering.

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Keywords: hiPSC, Hepatocyte, Maturation

TSC153

DECELLULARIZED URETERAL SCAFFOLD (PIG URETER) LOADED WITH ADIPOSE MESENCHYMAL STEM CELLS (SHEEP ADIPOSE TISSUE) PROMOTES URETER REGENERATION IN A XENOTRANSPLANT MODEL (SHEEP URETER)

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Ureteral injuries account for about 3% of urogenital traumas. Decellularized tissues have emerged as an alternative to ureteral repair, but the available protocols have failed in functional host integration. The aim of this study was to develop and validate in vivo a ureteral graft from a porcine ureteric scaffold, seeded with adipose mesenchymal stem cells (aMSCs). Ureteral samples from healthy pigs were used. Tissues were decellularized using Triton X-100 1% and SDS 0.1% under continuous intraluminal perfusion in a bioreactor designed by our group. Decellularization and structural integrity were characterized by histological analysis, β-actin western blot, residual DNA content, and scanning electron microscopy. Extracellular matrix (EMC) proteins and VEGF were studied by immunohistochemistry. Furthermore, 41 growth factors were analyzed by protein array. Recellularization was performed with aMSCs extracted from sheep adipose tissue, and it was evaluated histologically. Ureteral grafts were implanted into seven host sheep, and the functionality was analyzed by ureterography. At ten weeks, the implant was extracted, and integration was evaluated by histologically. Decellularized grafts showed high structural integrity and low DNA contamination and β-actin levels. EMC proteins and VEGF were observed. After cellularization with aMSC, the grafts showed the presence of groups of cells, and 32 growth factors were differentially detected. Sheep implants showed peristaltic movements and the regeneration of all ureteral tissue components. These results indicate that the protocol used is successful in achieving a decellularized ureter with an intact native architecture and recellularization with aMSCs. Also, the porcine ureteral scaffold seeded with aMSCs showed a high functional integration with the host tissue. Therefore, this type of graft may be a suitable alternative to ureteral regeneration.

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Keywords: Ureter, Decellularized scaffold, Xenotransplant