OMICS COUP 2nd World Congress on Conferences Accelerating Scientific Discovery Cell Science & Stem Cell Research

November 12-14, 2012 Hilton San Antonio Airport, USA

Therapeutic potential of placental mesenchymal stem cells after transplantation through portal vein into Chinese miniature pigs with acute liver failure

Hongcui Cao, Jinfeng Yang, Jiong Yu, Qiaoling Pan, Jianzhou Li, Pengcheng Zhou, Yanyuan Li, Jun Li,Yingjie Wang and Lanjuan Li Zhejiang University, P.R.China

Background: Stem cell-based therapy as a promising alternative approach to cure liver diseases is currently a focus of research worldwide. So far, preliminary studies of liver stem cell therapy have depended on rodent hepatic failure models. The purpose of this study was to generate mesenchymal stem cells from human placenta (hPMSCs) and determine their therapeutic potential for acute liver failure through establishing Chinese experimental miniature pig models in which liver failure is induced by D-galactosamine (GalN) separately through portal vein and jugular vein transplantation.

Methods: Adherent cells obtained from placentas were analyzed for their phenotype profile and adipogenic, osteogenic, and hepatic differentiation. To study the effectiveness and safety of hPMSCs for treatment of liver injury, 24 acute liver-failure (ALF) models of Chinese experimental miniature pigs were established and divided into four groups (n = 6/group): no cell transplantation; hPMSC transplantation via the jugular vein; X-ray-treated hPMSC transplantation via the portal vein; and hPMSC transplantation via the portal vein. Mortality rates, serum biochemistry, and histological and immunohistochemical analysis of liver tissues were determined 1–7 days after cell infusion and then every 2 weeks beginning at the second week until death.

Results: hPMSCs expressed high levels of CD29, CD73, CD13, and CD90 but not hematopoietic cell markers such as CD45, CD34, and CD133. hPMSCs had adipogenic, osteogenic, and hepatic differentiation potential, expressing ALB, AFP, CK18 and CK19, producing urea, storing glycogen and uptake LDL, exhibiting CYP-450 enzymatic activity, secretion LIF. hMSCs also stimulated PBMC producing IFN-γ by ELISpot assay . MTT assay indicated that treatment with X-rays inhibited cell viability. FACS assay indicated that dealing with X-rays inhibited cell proliferation, blocked cell cycle progression, and induced apoptosis. hPMSCs improved liver function *in vivo* after transplantation into the GalN-injured pig liver, as verified by changes in the levels of biochemical parameters. ALT, AST, ALP, CHE, TBIL, and TBA concentrations returned to normal levels after hPMSC transplantation. Meanwhile, histological findings (H&E staining) showed that transplantation of hPMSCs decreased liver inflammation, hepatocyte denaturation, and necrosis and promoted liver regeneration. This biochemical and pathological amelioration was not found in the other three groups. Additionally, hPMSC transplantation through the portal vein was able to significantly prolong survival compared with the other three groups. Histochemistry and RT-PCR for human ALB, AFP, CK18 and CK19, and PCR for human *alu* repeat sequences were confirmed the presence of human cells in the recipient liver (groups III, IV)

zjucaohc@163.com