DRUŠTVO ZA CELIČNO IN TKIVNO INŽENIRSTVO SLOVENIJE
CELL AND TISSUE ENGINEERING SOCIETY OF SLOVENIA

# 'Beyond Hematology – Cord Blood for Liver Intervention'

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Liver cirrhosis and/or liver malignancies have been nominated as the 5$^{th}$ leading cause of death worldwide. The WHO reported, in 2006, that 20 million people around the globe suffer from some form or other of severe liver illness. The ultimate fate of end-stage liver disorders is hepatic dysfunction and eventually organ failure. The only curative mode of management for liver failure is liver transplantation, which is subject to many limitations. Novel alternatives, such as artificial and bio-artificial support devices only aid in temporary replacement of some liver function until an organ is available for transplantation. These newer modalities also have drawbacks or remain experimental and still demand further controlled trials to allow proof of concept and safety before transferring them to the bedside.

Regenerative medicine and stem cell therapy has recently shown promise in the management of various human diseases. Recent reports of stem cell plasticity and its multipotentiality has raised hopes of stem cell therapy offering exciting therapeutic possibilities for patients with chronic liver disease. With the understanding that stem cells might not just be about making organs ex vivo, but also regenerating a patients own tissues; a concept is now developing to use stem cells to treat patients with serious disease conditions that are terminal or where conventional modes of treatment are insufficient. There exists a choice of stem cells that have been reported to be capable of self-renewal and differentiation to hepato-biliary cell lineages both in vitro and in vivo. These include: rodent and human embryonic stem cells, bone marrow haematopoietic stem cells, mesenchymal stem cells, umbilical cord blood stem cells, foetal liver progenitor cell and adult liver progenitor cells. It may, however, be argued that with a global population of 6 billion people and a global birth rate in access of 130 million per year, the products of birth ,umbilical cord and cord blood, possibly provide the most readily accessible and ethically sound alternative source of stem cells. The differentiated stem cells can be potentially exploited for gene therapy, cellular transplant, bio-artificial liver-assisted devices, drug toxicology testing and use as an in vitro model to understand the developmental biology of the liver.

In this study UCB-derived nucleated cells and umbilical cord-derived Mesenchymal stem cells were exploited for liver differentiation ex vivo. These cells were cultured on extracellular matrix (ECM) protein-coated dishes and inserted into ECM incorporated scaffold 3D culture systems. Stimulation with exogenous mitogens and morphogens to induce hepatic histogenesis was experimented. Immunofluorescence analysis revealed the expression of markers specific for: hepatic stem cells (CK-19), hepatoblasts (AFP) and mature hepatic and biliary epithelium markers including: albumin (ALB), and cytokeratin-18 (CK-18) and cytokeratin-19 (CK-19) and cytokeratin-7 (CK-7) respectively. The differentiated cells displayed several features of hepatic cell kinetics and metabolic activities, including glycogen synthesis, uptake of Indocyanine green dye and cytochrome P450 activity.

These cells may prove to have potential in developing cellular therapy for various liver disorders for which the current mode of therapy is inadequate and also provide an adequate in vitro model of parenchymal liver cells in toxicology and in bioartificial liver research.