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Isolation and Characterization of Stem Cells Sub Population within the Human Fetal Liver

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ABSTRACT

Human fetal liver is the potential source of both hematopoietic and non-hematopoietic stem cells which can be identified using phenotypic markers. Isolation of homogenous populations of hepatic progenitor cells and their sub-populations is an essential prerequisite for investigating specific markers and appropriate cell types for their possible clinical applications. Several studies have demonstrated the presence of a variety of stem cell populations within the fetal liver. The present study was undertaken to identify specialized cell populations, their valuable growth potential and bi-potential differentiation capability derived from human fetal liver using CD133.

Liver cirrhosis is characterized by distortion of liver architecture, necrosis of hepatocytes and regenerative nodules formation leading to cirrhosis. Various types of cell sources have been used for the management and treatment of decompensated liver cirrhosis. Knowledge of stem cells has offered a new dimension for regenerative therapy and has been considered as one of the potential adjuvant treatment modality in patients with end stage liver diseases (ESLD). Human fetal hepatic progenitor cells are less immunogenic than adult ones. They are highly propagative and challenging to cryopreservation. In our earlier studies we have demonstrated that fetuses at 10-18 wk of gestation age contain a large number of actively dividing hepatic stem and progenitor cells which possess bi-potent nature having potential to differentiate into bile duct cells and mature hepatocytes. Hepatic stem cell therapy for the treatment of ESLD is in their early stage of the translation. The emerging technology of decellularization and recellularization might offer a significant platform for developing bioengineered personalized livers to come over the scarcity of desired number of donor organs for the treatment of ESLD. Despite these significant advancements long-term tracking of stem cells in human is the most important subject nowadays in order to answer several unsettles issues regarding the route of delivery, the choice of stem cell type(s), the cell number and the time-point of cell delivery for the treatment in a chronic setting. Answering to these questions will further contribute to the development of safer, noninvasive, and repeatable imaging modalities that could discover better cell therapeutic approaches from bench to bed-side. Combinatorial approach of decellularization and nanotechnology

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could pave a way towards the better understanding in determination of cell fate post-transplantation.

The liver is a central metabolic and highly specialized detoxifying organ. Approximate 70%-75% of liver functions are being carried out by the hepatocytes which together with cholangiocytes (5%-10% of hepatic cells) constitute the liver parenchyma. Liver regeneration is a very rapid and well synchronized phenomenon. Liver responds to initial injury compensating the loss of parenchymal mass. If damage perseveres commencement of petite terminal peri-portal oval cells activates which engross mobilization of several vital factors.

Liver cirrhosis is characterized by distortion of liver architecture, necrosis of hepatocytes and regenerative nodules formation leading to cirrhosis. The available treatment modalities are not very effective against liver cirrhosis. Stem cells are considered one of the potential adjuvant treatment modalities in liver cirrhosis patients. Fetal hepatic stem cells transplantation in liver cirrhosis has emerged as an alternative to organ transplantation. However long-term stem cells labeling and tracking is needed for cell fate determination after transplantation. Decellularization technology provides a novel tool to develop bioengineered personalized livers to accomplish the shortage of donor livers.

Stem cells labeling and tracking in human tissues/organs is the most important subject nowadays in order to answer several unsettled issues regarding the cell delivery routes, stem cell choice, number of cells to be infused and the time-point of cell delivery for the treatment in a chronic setting. Answering to these questions will further contribute to the development of safer, non-invasive, and repeatable imaging modalities that could discover better cell therapeutic approaches from bench to bed-side. Long-term monitoring of transplanted stem cells continuously with high temporal resolution and good biocompatibility will allow us to better understand the precise regeneration mechanisms in different organs. Nanobiotechnology has emerged as the most immense area for labeling and tracking of cells both in vitro and in vivo.

Keywords: Human hepatic progenitor cells; CD133, Sub-population; Coexpression