2ND INTERNATIONAL CONFERENCE ON CELL SCIENCE AND REGENERATIVE MEDICINE

Zeeshan Afzal[1], Mekhola Hoff[1], Simon Harper[1], **Emmanuel Huguet[1*]**

1 Cambridge University, Department of Surgery, Addenbrookes Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge NIHR Biomedical Research Centre, Hills Road, Cambridge CB20QQ, UK

Portal venous repopulation of decellularised rat liver scaffolds with syngeneic bone marrow stem cells

Abstract: Liver transplantation is the only life-saving treatment for end-stage liver failure but is limited by the organ shortage and consequences of immunosuppression. Repopulation of decellularised scaffolds with recipient cells provides a theoretical solution, potentially allowing reliable and timely organ sourcing without immunosuppression. Recellularisation of the vasculature of decellularised liver scaffolds was investigated as an essential prerequisite to the survival of other parenchymal components,and with a focus on Liver Sinusoidal Cells (LSECs) given their central role in global hepatic function.

Rat liver decellularisation was carried out by portal vein (PV) perfusion using a detergent-based solution. Scaffolds were perfused via the PV with culture medium at 37°C and infused with primary bone marrow (BM) stem cells. BM stem cells were assessed for key marker expression using fluorescence-activated cell sorting (FACS), and recellularised scaffolds analysed by light (LM), electron (EM) and immunofluorescence (IF) microscopy. Recellularised scaffolds changed in macroscopic appearance from a translucent to an opaque structure by day 30. Stem cells engrafted in portal, sinusoidal and hepatic vein compartments on LM with cell alignment reminiscent of endothelium on EM. Engrafted cells expressed LSEC endocytic receptors (mannoseR, FcR and stabilinR), and cell surface marker expression altered following engraftment from a haematopoietic (CD31- CD45+) to an endothelial phenotype (CD31+ CD45−) on FACS and IF.

This is the first report of BM stem cells used to repopulate decellularised liver. This approach is clinically relevant as the cells are recipient specific, sourceable in relevant numbers, and not subject to oncogenic concerns that relate to cell lines or induced pluripotent stem cells. These results represent a step towards complete recellularisation of liver vasculature and progress towards generation of transplantable neo-organs.

Keywords: Bone marrow stem cell, decellularisation, liver, recellularisation, scaffold, vasculature

Biography: Emmanuel Huguet is a Consultant Liver Transplant and Hepato-Pancreato-Biliary surgeon at Addenbrookes Hospital, Cambridge University, a fellow of the Royal College of Surgeons of England, and International Hepato-Pancreato-Biliary Association member. He completed his medical degree in Bristol, and subsequently undertook a PhD in cancer molecular biology at Oxford University in the Institute of Molecular Medicine, John Radcliffe Hospital. He carried out surgical training in Oxford, the Centre Hepatobiliaire Paul Brousse Hospital in Paris, and Cambridge, where he now leads liver metastasis surgery. Alongside clinical duties, he has an interest in regenerative medicine and directs research in decellularised liver scaffolds repopulation.