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Ultrasound guided injection of murine and rat hepatic portal vein for surgical refinement in type 1 diabetes studies is not a viable alternative technique

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Clinical islet transplantation for Type 1 diabetes (T1D) is performed using ultrasound guidance (US) via percutaneous trans-hepatic portal venous access. Injection of islets and other substances into the hepatic portal vein (HPV) of mice using open laparotomy techniques are commonplace when researching T1D therapies. However, this procedure is invasive, leads to longer recovery times and increases potential for infections. Techniques using open laparotomy do not resemble procedures seen in clinical settings. US injection into the HPV mostly negates the above concerns, and better emulates clinical methods of islet transplantation in humans.

Hypothesis: US methodologies will refine surgical procedures, improving recovery and welfare of animals, whilst seeing the same number and distribution of cells/markers as when using open laparotomy surgical techniques.

Methodology: US and open laparotomy HPV injections were performed in female C57Bl/6-mice and US HPV injection was performed in male RNU-rats (injecting 0.1 mg of 20 um fluorescent PLGA microparticles to aid analysis). Tissues were cryopreserved at 24 hours post-transplant and subsequently cryo-sectioned. DAPI staining alongside the fluorescent microparticles allowed for the quantification of microparticles in the liver tissues following each surgical technique.

Results and Conclusions: US injection results in a significant reduction of microparticles in liver tissues, when compared to open laparotomy surgical techniques. Clustering of microparticles around the edge of tissues is seen in animals having undergone US techniques, suggesting that microparticles are residing where the needle is being withdrawn through the liver or accumulating around tissues if the injection releases into the body cavity. Locating and accurately injecting into the HPV using ultrasound guidance may hinder the success of transplants in rodent models. Reflux of some microparticles out of the vein where the needle is inserted is seen upon commencement of the injection.

US HPV injection is therefore not a robust or reliable method for such studies.

Recent Publications

1. Walker, S., M. Appari, and S. Forbes, Considerations and challenges of islet transplantation and future therapies on the horizon. Am J Physiol Endocrinol Metab, 2022. 322(2): p. E109-E117.
2. Alwahsh, S.M., et al., Fibroblast growth factor 7 releasing particles enhance islet engraftment and improve metabolic control following islet transplantation in mice with diabetes. Am J Transplant, 2021. 21(9): p. 2950-2963.
3. Cantarelli, E., et al., Murine animal models for preclinical islet transplantation: No model fits all (research purposes). Islets, 2013. 5(2): p. 79-86.
4. Zaw Thin, M., et al., Stem cell delivery to kidney via minimally invasive ultrasound-guided renal artery injection in mice. Sci Rep, 2020. 10(1): p. 7514.
5. Xia, C., et al., Ultrasound-Guided Transplantation of Mesenchymal Stem Cells Improves Adriamycin Nephropathy in Rats Through the RIPK3/MLKL and TLR-4/NF-kappaB Signaling. Stem Cells Dev, 2021. 30(20): p. 1003-1016.

Biography

Sophie Walker was awarded a 1st class MChem BSc in Chemistry with year in industry from the University of Leeds (2015-2019). Following on from undergraduate studies, she moved to the University of Edinburgh Centre for Cardiovascular Science at the Queen's Medical Research Institute to study for a MSc (2019-2020) and PhD (2020-present) funded by the British Heart Foundation. Here, she is studying to optimize islet transplantation for the treatment of type 1 diabetes through the use of microparticles to modulate the liver niche, working under the supervision of Prof. Shareen Forbes, Dr Mairi Brittan, and Dr Lisa White (University of Nottingham). This work will hopefully allow for a greater insight into the effect of the liver niche on the survival of islet cells when transplanted via hepatic portal vein injection and aim to provide information to aid the continued development of the procedure with its translation into a clinical setting.

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