ESOT Transplant Fellowship – Research progress report

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Progress Report: Since commencing my research residency in June 2023, supported by the ESOT Transplant Fellowship, I have made significant strides in my project at the Centre for Regenerative Medicine at the University of Edinburgh, UK. This report outlines the key steps taken throughout the project, the current stage of research, and the progress toward the proposed goals.

Research Overview and Achievements: Under the guidance of Dr. Sofia Ferreira-Gonzalez and Prof. Stuart Forbes, I have developed valuable preliminary data that was crucial during my PhD interviews. This data played a significant role in securing a highly competitive, fully funded PhD scholarship in Regenerative Medicine at the University of Edinburgh, starting in October 2024. My PhD research will focus on reconditioning discarded human donor livers using machine perfusion, a critical step toward my goal of becoming an academic transplant surgeon.

Project Progress: My primary focus has been on investigating biliary complications (BC) post-liver transplantation using an assessment tool developed by Dr. Sofia Gonzalez and her team, named Sensibile. This tool is designed to predict the likelihood of biliary complications in potential liver grafts, providing surgeons with critical insights before transplantation. Throughout the project, we have optimized the application system to ensure the proper flow of bile within the tool, utilizing 3D printing technology. Additionally, we have tested human bile samples to refine this point-of-care test, with the goal of enabling earlier recognition and treatment of BC.

Skills Acquired: Throughout the fellowship, I have acquired a diverse skill set, including proficiency in tissue culture techniques, extensive work with 3D organoids and 2D cell cultures, and expertise in histology, microscopy, biochemical assays, and PCR for real-time assessment of perfused livers. Additionally, I obtained a Personal License for animal work in the UK, which allowed me to engage immediately with animal research packages.

Collaborations and Future Directions: We have also established a fruitful collaboration with the Luc van der Laan group in Rotterdam, focusing on the study of Primary Sclerosing Cholangitis (PSC) organoids. My work has centered on characterizing PSC livers in comparison to healthy liver grafts. The investigation into the role of senescence in PSC livers is ongoing, with preliminary data indicating that cellular senescence is a key feature of this disease. Currently, we are preparing to send these samples for single-cell sequencing, with the long-term goal of exploring how senolytic drugs interact with PSC grafts during normothermic machine perfusion (NMP). Additionally, we aim to understand how senescent cells interact with macrophages, potentially testing therapeutic interventions with senolytics and macrophages. This will inform future biosignatures that will be measured using the sensibile tool, which could potentially open new avenues for the detection of other liver-related conditions that require a liver transplant.

Current Stage and Proposed Goals: At this stage, the project is progressing well, with significant achievements in data collection, skill acquisition, and collaborative efforts. The next steps involve advancing our understanding of senescence in biliary complications and PSC livers and testing potential therapeutic interventions. The fellowship has effectively prepared me for the upcoming PhD endeavor, and I am actively pursuing additional funding opportunities to ensure the seamless continuation of this pivotal work.

In conclusion, I have met the proposed goals thus far, and the project is on track to achieve its long-term objectives. The collaborative environment at the Centre for Regenerative Medicine, particularly within the Forbes Lab, has been instrumental in facilitating this research. I am deeply grateful for the invaluable financial support from the ESOT Transplant Fellowship, which made securing this PhD possible. I am also very thankful for the support and resources provided by both the Innsbruck Transplantation Center and the Centre for Regenerative Medicine. I eagerly anticipate the next phase of this research journey and the continued pursuit of innovative solutions for hepatic complications.