CAF/24/03 - PRECISION ATLAS OF PANCREATIC CYSTS: Determining the molecular and cellular characteristics of premalignant pancreatic lesions at high-risk of progression to cancer using spatial-omic strategies

Pancreatic ductal adenocarcinoma (PDAC) continues to be associated with extremely poor survival. Prompt investigation, diagnosis and treatment are essential for cure. 15% of PDAC's develop from pancreatic cysts representing an opportunity to diagnose early and prevent cancer developing. Widespread use of CT and MRI scans has increased discovery of cysts, however, the risk of cancer developing within a cyst remains difficult to determine. The best way to deal with these cysts remains challenging and requires frequent hospital visits and costly scans for monitoring. The stakes are high, as while pancreatic cancer has a poor survival, pancreatic surgery to remove the cyst carries significant risk including death.

There is an urgent need for 1)New approaches to improve understanding how pre-cancerous pancreatic cysts develop into cancer 2)New methods to select patients with cysts who will benefit most from surgery and those who can be safely watched. We aim to study pre-cancerous pancreatic cysts in unprecedented detail to better understand the reasons cysts develop into cancer. Previously, to measure which genes were 'switched-on', tissue samples were digested and so the 'geography' of tumour and immune cells position on the 'battlefield' was lost. We have a multi-pronged approach to overcome this challenge.

The planned research will study surgically removed pancreatic cyst tissue from patients using latest molecular microscopes designed to work with fixed tissue, to understand how individual cells of human pre-cancerous cysts, communicate with surrounding immune cells and evolve into cancer. High powered computer and artificial intelligence analysis techniques will enable us to unlock the interactions between the neighbourhoods of cells enabling us to draw the most detailed 3D map of pre-cancerous pancreatic lesions and describe what the cells are saying to each other. We will investigate differences in cell populations in different types of cysts, including those which are 'far' and 'near' to becoming a cancer. These results will be combined with MRI scans and fluid sampled from cysts to help identify 'high-risk cysts' that require surgical removal to prevent cancer developing. The results of this research will be published in scientific journals as well as on social media and other communication channels to ensure that our findings reach as wide an audience as possible.

The team performing this work come from a range of scientific and medical backgrounds and have a long and fruitful history of working together. They are in fact world leaders in this field of molecular microscopes. To ensure we have enough samples to make genuine discovery, we have generated a pancreatic cyst network from USA, Australia, and Europe willing to share tissue samples.

The team has all the necessary support and experience to perform this project and have successfully accomplished similar research studying cancer from patients in Scotland. If successful, this project will provide new understandings of how and what pancreatic cysts evolve into pancreatic cancer. The findings of this work will provide important information which will guide patient selection for pancreatic cysts to ensure ‘low risk’ patients can be reassured and limited NHS resources saved. Detecting those ‘high-risk’ cysts by studying the fluid has potential to revolutionise care for this condition by focusing surgery on those patients who need it as well as facilitate new drug development to halt cancer developing in the cysts, new drugs to treat pancreatic cancer and ultimately improve outcomes for patients preventing deaths for patients in Scotland.