This 4-year PhD studentship will be based initially at the Cancer Research UK Manchester Institute, Alderley Park, Cheshire. The rebuilding of our world class research facilities is well underway, and we anticipate returning to our original site in Withington, Manchester, UK in 2023 next to the Christie NHS Foundation Trust

Despite being the 11th most frequent occurring cancer, Pancreatic Ductal Adenocarcinoma (PDA) is currently the 4th leading cause of cancer-related deaths and projected to be the 2nd leading cause by 2030.

A characteristic feature of PDA is a pathological remodelled desmoplastic reaction, which takes up more than 80% of the tumour volume on average. Host stromal cells such as fibroblasts and immune cells are conscripted by tumour-cell signals to enable tumour growth and immune escape. Moreover, a remodelled extracellular matrix alters tissue biophysics resulting in a stiff, poorly perfused, nutrient depleted environment. While the tumour stroma largely has been viewed as tumour promoting, emerging data have demonstrated that stromal subsets act in a tumour-restrictive manner. The mechanisms whereby individual stromal subsets regulate tumour progression or restriction is less well understood. Determining the molecular mechanisms of promoting and restrictive stromal subsets is crucial to the development of stromal targeted therapies.

The Systems Oncology lab has a long-standing interest in understanding tumour-stroma interactions and how these interactions regulate tumour cell function. The aim of this project is to define and characterize mechanisms whereby the tumour microenvironment balances tumour progression or regression and to determine how individual tumour cells bypass these signals. The project involves use of in vivo animal models, 3D ex vivo organoid models as well as human PDA samples, which will be analysed by a combination of proteomics (mass spectrometry), single cell analysis (CyTOF) and functional genetic manipulation.

University of Manchester entry: September 2022