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Project Title	**"Characterising tumour-promoting and restrictive populations of fibroblasts"**
Group Leader	Claus Jorgensen
Research Group	Systems Oncology

This 4-year PhD studentship will be based in our new world class research building next to the Christie NHS Foundation Trust, Withington, Manchester, UK.

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. We recently identified two distinct populations of cancer-associated fibroblasts with tumour permissive and restrictive functions (Hutton et al Cancer Cell 2021). The aim of this project is to define and characterize mechanisms whereby naïve and cancer associated fibroblasts regulate tumour progression or regression. Specifically, we aim to determine how tumour permissive and restrictive populations of fibroblasts interact with the immune system to ultimately control tumour progression. 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.