Project Details	
Project Code	MRC23IIAREx Scholpp
Title	Quantitative Analysis of Wnt Signalling in the Gastric Tumour Microenvironment
Research Theme	Infection, Immunity, Antimicrobial Resistance and Repair
Summary	Gastric cancer is a multifactorial disease-causing over a million deaths yearly. Deregulation of oncogenic cell signalling, such as the Wnt signalling pathway, leads to tumour growth and metastasis. In this project, the student will apply novel microfluidic tools to decipher the function of Wnt signal spreading and activation in the tumour microenvironment to develop effective new therapeutics to combat gastric cancer.
Description	Gastric cancer is the fifth most common cancer and the third leading cause of cancer-related deaths worldwide. There is an urgent need to develop novel therapeutic approaches to improve prognosis. A complex interplay in the tumour microenvironment promotes gastric cancer development. Deregulation of oncogenic cell signalling pathways such as the Wnt signalling pathway leads to the acquisition of malignant phenotypes, including tumour growth and metastasis. Mutations in Wnt-related tumour suppressor genes are closely associated with transforming normal gastric epithelium into adenomas. Concomitantly, elevated expression of Wnt ligands and receptors is essential for tumour progression. However, Wnt ligands and receptors are only expressed by a few cell types within the tumour tissue. Thus, there is a pressing need to improve our understanding of Wnt dissemination within a tumour. Recently, we have broken new ground by showing that signalling filopodia, known as cytonemes, transport Wnt proteins in tissues (Stanganello et al., 2015, Nat Comms; Mattes et al., 2018, eLife; Brunt et al. 2021, Nat Comms). Our preliminary data suggest that cancer-associated fibroblasts and tumour cells produce different Wnt ligands and receptors. However, both use the same complex cytoneme network to disseminate and receive these signals in the tumour microenvironment. This discovery is potentially game-changing because it demonstrates the importance of the tumour cytoneme network and targeting this network could allow us to control signalling, hence tumour behaviour. In this project, the student will apply novel microfluidic tools to elucidate the exact function of Wnt cytonemes in the tumour microenvironment, specifically in gastric adenomas. Focusing on cancer-associated fibroblasts and gastric cancer cells, the student will develop a high-throughput method to screen for effective new therapeutics and characterise unknown tumour signalling properties. Concomitantly, the student will test for the function of Wnt signalling in the promotion of gastric cancer stemness, thus developing and optimising individual treatment regimes. In summary, we believe the outcomes of this project will fundamentally change our understanding of signalling in gastric cancer and provide novel and effective tools to study tumour microenvironment interactions in individual cancers.
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