

EPD/25/14 - Preventing colorectal cancer through assessment and manipulation of pre-cancer adenoma and early cancer immune contexture

Background:

Colonic polyps are benign growths found in the bowel which can become cancerous over time. When we find polyps during colonoscopy, during bowel screening for example, we can remove them to prevent future bowel cancers. People who have polyps removed remain at risk of future polyps or bowel cancer so some are recommended repeat surveillance colonoscopy as we do not have any other way to prevent them. However, the methods we currently use to try and predict such people's future risk are basic and inaccurate. This means that many people who do not go on to get polyps or cancer undergo unnecessary colonoscopies. These procedures are unpleasant, invasive, and have associated risk. They are also costly to the NHS, the environment and our economy / wider society. The NHS is currently struggling to keep up with demand for colonoscopy and so those who actually are at higher risk of future polyps or cancer can find it difficult to get the high quality surveillance they need.

Research aims:

My research is focussed on both improving our ability to predict the risk of developing future polyps or cancer for patients who are found to have polyps at colonoscopy, and at identifying other ways in which we might reduce the future risk, e.g. by diet or medication. I have already built a bank of samples of polyps removed from patients during bowel screening colonoscopy. My initial work suggests that the immune cells in polyps are related to future polyp and cancer risk, however at present I have limited detail of why this is the case. In this fellowship I aim to better understand the different types of immune cells within polyps which confer risk of future polyps or cancer and understand the interactions between them and the polyp cells. I want to understand whether immune changes are limited to those polyps which we have removed, or whether they are also found in other polyps removed at the same time, later during surveillance, or even in the rest of the colon. If this is the case it might explain why the immune cells in a polyp which has been removed, can tell us about future polyp and cancer risk.

Methods:

I will examine the immune cells in polyps from my existing tissue bank, which includes polyps removed at index bowel screening colonoscopy between 2009-2016 in NHS Greater Glasgow and Clyde. I will compare patients who did or did not have a further polyp or cancer at surveillance colonoscopy up to 6 years later. I will use detailed tests of the polyps which will tell me the type, number and location of the immune cells within the polyps (multi-plex immunofluorescence) as well as what the immune cells are doing (spatial transcriptomics), creating a high risk ""signature"". I will also recruit patients with and without polyps from my colonoscopy list, and take biopsies from the normal colon near, and far away from the polyps. I will then look at these "normal" biopsies using the same techniques to look for those same high risk immune signatures. I will survey recruited patients to determine how acceptable the additional biopsies were to them, informing future work.

Benefit to patients:

Identifying specific immune cell types and interactions which drive polyp and cancer formation will allow us to better predict future polyp or cancer risk, allowing us to improve surveillance for patients with polyps, reducing unnecessary costly and invasive colonoscopy. Targeting risk-conferring immune cells in polyps and the wider colon in prospective studies and early clinical trials of the highest risk patients may eventually allow us to prevent colorectal cancer.