SCAF/16/01 - Targeting the intestinal stem cell niche through energy and metabolism signalling via the mTOR for colorectal cancer chemoprevention

Bowel cancer, the second leading cause of cancer deaths in the UK, has a considerable preventable component (~54%). Risk factors include diabetes, obesity, and metabolic syndrome and highlight the strong link between metabolism, diet and bowel cancer. Given the national increase in obesity, we need to understand the ways in which nutrient (food) overload can lead to bowel cancer. We think that excessive nutrients lead to bowel cancer by increasing certain types of cells called stem cells. Cells communicate with each other through signals that tell a cell how to behave. An important regulator of such cell signals is the mTOR molecule, which changes the bowel stem cell response to nutrients to maintain normal activity. The mTOR cell signalling pathway is progressively abnormal in bowel cancer development. We know that common drugs like aspirin and metformin decrease the risk of getting bowel cancer and may decrease stem cells. Hence, there is powerful rationale to study how known bowel cancer preventive agents may reset abnormal metabolism and stem cells.

We have previously showed that aspirin blocks the mTOR signal in bowel cancer cells. Our Scottish population data show that aspirin will not prevent bowel cancer in all people taking these drugs and so it is important to identify who will respond so we can get the ‘right drug’ to the ‘right patient’. In this study patients will be given aspirin or metformin or both and blood and bowel lining will be sampled to identify metabolic targets of the drugs and effects on the stem cells. CSO funding will enable us to undertake important metabolic studies to define biomarker response profiles to aspirin and metformin that indicate whether a person may benefit from the cancer prevention properties of these drugs. This research is highly relevant to the long-term goal of bowel cancer prevention, a national health priority research theme.