

TCS/23/12 - Identifying novel treatment targets for bile acid diarrhoea through interrogation of targeted epithelial barrier disease mechanisms and discovery science proteomics in human gut organoid models

Bile acid diarrhoea (otherwise known as BAD) occurs in 1 in 100 people in the UK, with approximately 50,000 cases in Scotland. It can occur with no explanation or after an operation to remove the end of the small bowel, when the gallbladder is removed or after some cancer treatments. It can also be associated with inflammation in the small bowel or with irritability of the bowel (known as IBS). Symptoms can be severe and include frequent watery diarrhoea with urgency and uncontrolled leakage (incontinence), stopping a person leaving the house, travelling, working, and socialising, leading to isolation. Current treatments are limited and are not effective for all. The changes in cell biology underpinning this condition are not fully understood. This project investigates how bile in the large bowel affects the cells lining the gut using 3D mini gut structures (called organoids) created from human bowel tissue. We will characterise changes in the structure and behaviour of the gut cells by assessing genes, amount and function of different proteins, the structure of the mucus, the leakiness of the barrier and how injury is repaired in response to bile. Overall, we hope to identify exciting new knowledge of why bile acid diarrhoea develops and identify new ways of treating this condition. A new treatment will offer a real-life difference to patients with BAD.