TCS/19/18 - Understanding resistance to targeted therapies in oesophageal squamous cell carcinoma as a foundation for developing new precision medicine approaches

Oesophageal squamous cell carcinoma (OSCC) is a type of cancer of the oesophagus (food-pipe), associated with social deprivation and poverty, and a key public health concern for Scotland where the incidence in women is the highest in the world. Current treatments are not very effective and most patients die within 1 year. Our previous research suggests that OSCC patients who have tumours with too much of the EGFR protein benefit from drugs which specifically block EGFR and stop EGFR-positive tumours growing. This research lays the foundations for personalised precise treatment. However, all OSCC tumours eventually become resistant to anti-EGFR drugs and tumours regrow. To overcome this major barrier to effective treatment we have carried out laboratory studies which show that resistance to EGFR inhibitors is often linked to the action of proteins in the PI3K/AKT/mTOR pathway which help tumour cells survive during anti-cancer treatment. Combining medicines to block both EGFR and PI3K/AKT/mTOR at the same time could improve treatment for OSCC patients and overcome drug resistance. This project extends our previous studies to provide the data needed to deliver clinical trials using our established research networks and will accelerate the development of effective, personalised and precise treatments for OSCC patients.