Oesophageal cancer has increased in incidence globally almost 6-fold over the last 30 years. There are approximately 450 cases per year in Ireland, with almost 400 deaths, highlighting that it presents usually at an advanced stage and is difficult to cure.

The integration of science and medicine defines the model of best cancer care in the leading comprehensive cancer centres internationally, and to this end Trinity College Dublin aligned with St James’s Hospital in February 2017 formally launched a combined initiative to develop a Cancer Institute founded on such principles, unique for Ireland, and rich in research opportunity. Trinity’s Department of Surgery at St James’s Hospital has a particular focus on translational oesophageal cancer research. The hospital is the National Centre for Oesophageal Cancer, and translational research in premalignant and malignant disease of the oesophagus is a major theme within the Trinity Translational Medicine Institute (TTMI). Some key themes are as follows:

**Obesity and cancer** – Oesophageal cancer is an obesity-associated cancer, particularly in men, and especially related to central obesity (‘belly fat’), as well as associated type 2 diabetes, and fatty liver. Excess unhealthy fat can drive inflammation and fuel cancer development, and we have shown than this ‘belly fat’ is a hive of increased activity of immune cells and can alter the energy metabolism of cancer cells allowing them to remain immortal.

**Inflammation to cancer: The role of reflux**

Most oesophageal cancer arises in the context of symptoms of excessive acid and bile causing heartburn and reflux. About 10% of such sufferers acquire an identifiable change in their oesophagus known as Barrett’s oesophagus which may be pre-malignant. We lead a National Barrett’s Registry and Biobank which links six Irish hospitals to better understand the clinical management and disease progression rates of this disease model to inflammation causing cancer, and to develop scientific tests to predict which patients will progress to cancer. We have shown that alterations in immune cell function, energy metabolism and genomic instability have the potential to distinguish patients at high risk, permitting precision management and the potential of novel targeted therapies.

**Increasing cure rates using novel diagnostic and therapeutic platforms (theranostic programme)** – Patients with oesophageal cancer typically undergo chemotherapy, alone or combined with radiation therapy, prior to surgery. Less than half benefit meaningfully from this pre-surgery therapy, so the ability to predict response has enormous application in improving outcomes through predictive modelling and personalised medicine. A recent article from our group highlighted the importance of a microRNA (miR-17) in cancer stem cells in controlling radiation response. We are currently investigating whether adding a synthetic miR to radiotherapy enhances effectiveness. In addition, in collaboration with a company in New York (miR Diagnostics), we have developed a microRNA signature which is being tested across multi-sites for its sensitivity and specificity in segregating patients with good and poor response to radiation and chemotherapy prior to surgery. We are leading an international randomised clinical trial (NeoAEGIS) of 600 patients, coordinated through Cancer Trials Ireland, and involving international scientific partnerships including Cambridge University and Imperial College London. Our drug discovery therapeutics programme has identified and patented novel dual action drugs that act as radiosensitisers and can potentially help patients resistant to therapy by specifically targeting blood vessels (Figures 1 and 2) and energy metabolism levels in cancer cells.

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Improving the patient journey – There is no more complex cancer operation than removal of the oesophagus, which carries a high risk of morbidity. In collaboration with the Discipline of Physiotherapy we have developed programmes, conducted at the Wellcome/Health Research Board clinical research facility, targeting the optimisation of patients’ physical wellbeing and conditioning though prehabilitation (PREPARE trial), and rehabilitation following treatment and extending into survivorship (ReStOre trial).
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