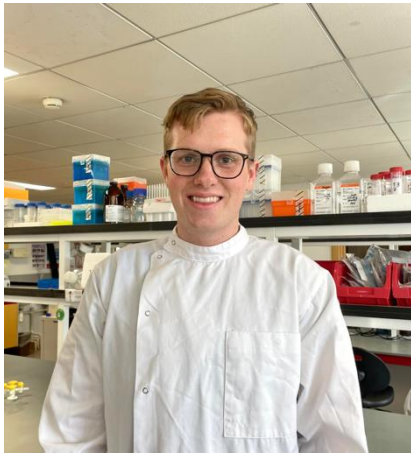


ImmunoTools *special* Award 2025



Sam Cahill, PhD-student

Lab: Professor Joanne Lysaght, PhD

Cancer Immunology and Immunotherapy Group,
Department of Surgery, Trinity Translational Medicine
Institute, St. James's Hospital Campus, Dublin 8, Ireland

Determining the role of immune checkpoint signalling in the progression of premalignant Barrett's oesophagus to oesophageal adenocarcinoma: expanding the target cohort for immune checkpoint inhibition.

Background:

Oesophageal cancer is the 9th most common cause of cancer and the 6th leading cause of cancer deaths worldwide. The two main types of oesophageal cancer are squamous cell carcinoma (SCC) and oesophageal adenocarcinoma (OAC). While the rates of SCC have been steadily reducing worldwide, OAC numbers continue to increase, particularly in developed countries. OAC is a dismal prognosis cancer with a 5-year survival rate of approximately 20%, largely attributable to its late stage of diagnosis. Its precursor condition, Barrett's Oesophagus (BO) is an obesity-associated condition resulting from gastroesophageal reflux disease (GORD), which raises a patient's likelihood of developing OAC by up to 125 times. Initially, GORD was believed to induce BO through the acidic damage caused to the oesophageal tissue. However, its aetiology is now understood to involve the inflammatory processes resulting from GORD. The current treatment landscape for BO is quite limited, including proton pump inhibitors, radio-frequency ablation and cryo-ablation. This highlights the need for preventative approaches to malignancy.

Immune checkpoint signalling molecules are essential components to the function of the immune system, crucial in maintaining immune homeostasis. Dysregulated immune checkpoint signalling is commonplace for many cancer types, driving tumour development by enabling immune system evasion. Targeting these dysregulated molecules with immune checkpoint inhibitor therapies has revolutionized cancer treatment, in some cases offering long-term remission in previously untreatable cancers. However, little is known about the role of immune checkpoint signalling in the premalignancy setting. Our group has previously

outlined immune checkpoint expression on the surface of epithelial cells across the progression from normal to BO and OAC, however their role in disease progression is yet to be understood.

This project will also investigate the role of galectin-3, an important immunomodulatory lectin, on the expression of immune checkpoint signalling and cell adhesion markers, as well as its relationship with TGF- β . Galectin-3 has shown to have immunomodulatory roles but little is known about its role in BO progression. Murine models have outlined the synergistic effects of galectin-3 with immune checkpoint inhibitors, but little is known about the relationship between galectin-3 and immune checkpoint signalling in the context of BO.

Research Hypothesis:

Immune checkpoint signalling plays an important role in the disease progression from normal oesophagus to BO and OAC. Galectin-3 plays an important role in the inflammatory response underpinning the disease progression.

Research Objectives:

To uncover the role of immune checkpoint signalling and galectin-3 across the disease progression of BO and whether these signalling pathways can be modulated to prevent disease progression to malignancy.

Methodology:

The work carried out in this project will use Immune checkpoint and immunophenotyping markers to analyse the levels of immune signalling in both epithelial cell lines of disease progression and T-cells. It will also assess the importance of galectin-3 in the progression of BO with respect to immune checkpoint signalling and cellular adhesion on both immune and epithelial cells and whether there is an inverse relationship between TGF- β levels and galectin-3. In order to assess the relationship between galectin-3 and its effect on disease progression through immune checkpoint signalling and adhesion, the following markers and recombinant proteins (supplied by **ImmunoTools**) will be used:

ImmunoTools *special* AWARD for **Sam Cahill** includes 10 reagents

FITC - conjugated anti-human CD18, CD69

PE - conjugated anti-human CD3, CD4, CD11a, CD279

APC - conjugated anti-human CD8, CD66

recombinant human cytokines: rh GAL-3, TGF-beta1

[DETAILS](#) more [AWARDS](#)