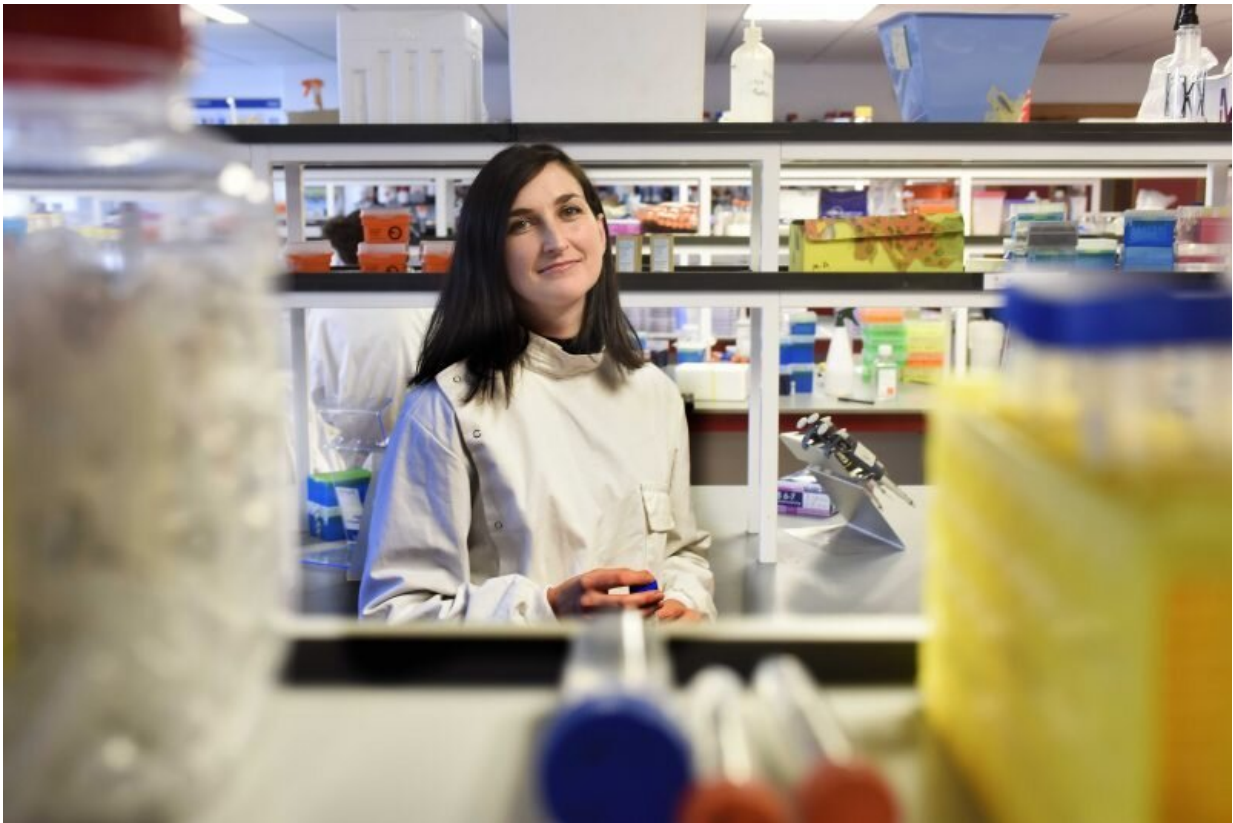


Researchers identify cancer killing capability of lesser-known immune cells

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Research Assistant Professor at TTMI and Principal Investigator, Dr Margaret Dunne. Credit: Moya Nolan.

Researchers at Trinity College Dublin have identified, for the first time in oesophageal cancer, the cancer killing capability of a lesser-known

type of immune cell, presenting a new potential therapeutic target. Their research has been published today Wednesday, July 10th 2019 in the international journal *Frontiers in Immunology*.

Oesophageal cancer is a very aggressive type of cancer with poor prognosis, and the 5-year survival rate is typically less than 15%. Linked with obesity, oesophageal cancer is one of the fastest growing cancers in the Western world and incidence is due to double in Ireland within the next few decades. Current treatment strategies work well but only for a minority (approx. 25%) of patients so new treatment options are urgently needed.

New treatment strategies targeting the [immune system](#) have had revolutionary effects in other cancer types, but the latest clinical trials show that, disappointingly, immunotherapy offers no real benefit for the majority of patients with oesophageal cancer.

The Cancer Immunopathology research team from the Trinity Translational Medicine Institute (TTMI) based in St James's Hospital, are studying unconventional types of immune cells with lesser known functions. T cells (a type of white blood cell) are very important in fighting cancer; preventing tumours arising and killing off established tumours if activated in the correct way. Up until now, the majority of immune-based studies have largely focused on conventional CD8 (cytotoxic) T cells, but unconventional T cells, although less abundant, can also have potent cancer killing ability.

The team investigated a particular type of T cell, known as a MAIT cell (mucosal-associated invariant cell) in oesophageal cancer. MAIT cells are known to protect against bacterial infections but little is known about what they do in cancer.

The team at Trinity are the first to report the characterisation of MAIT

cells in the oesophageal cancer setting. They looked at MAIT cells blood and tumours from patients with oesophageal cancer or a pre-cancerous disorder called Barrett's Oesophagus, and found that:

- MAIT cells are decreased in the blood of cancer patients, compared to healthy donors but are found in oesophageal tumours at higher levels than healthy tissues.
- MAIT cell levels are not affected by chemoradiotherapy treatment, unlike other T cell types.
- Healthy MAIT cells can kill [oesophageal cancer](#) cells in a [test tube](#), but this killing is reduced when liquid from fresh tumour biopsies is present, meaning that factors from the tumour can prevent MAIT cell killing.
- MAIT cells taken from oesophageal tumours showed high levels of markers associated with functional inhibition. This means that oesophageal tumours seem to be able to stop MAIT cells from killing them, by using these inhibitory markers to deliver a "do not kill" signal.

Overall, these results reveal an anti-tumour function for a new potential therapeutic target cell in this aggressive cancer type, which is being inhibited by the tumour itself. Finding new ways to reverse the inhibition of MAIT cell tumour-killing ability may offer a new therapeutic strategy in the fight against cancer.

Research Assistant Professor at TTMI and Principal Investigator, Dr. Margaret Dunne said: "Oesophageal cancer rates are rising in Ireland, and improved treatment strategies are urgently needed. By revealing how lesser studied immune [cells](#) work in cancer, we can better understand the shortcomings of current immunotherapies and investigate new ways to boost the anti-cancer immune response."

"Immunotherapies have revolutionised [cancer](#) treatment but still only

work for a minority of people. A more in-depth understanding of underlying biology will be critical to unravel why this is—and to allow more patients to benefit" she added.

More information: Ashanty M. Melo et al, Mucosal-Associated Invariant T Cells Display Diminished Effector Capacity in Oesophageal Adenocarcinoma, *Frontiers in Immunology* (2019). [DOI: 10.3389/fimmu.2019.01580](https://doi.org/10.3389/fimmu.2019.01580)

Provided by Trinity College Dublin

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