ImmunoTools *special* Award 2018

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Delineating the role of natural killer cells in obesity-associated cancer

My research examines how we can target the underlying immune processes in pathological inflammation in obesity, cancer and liver disease. Specifically, my studies address how chemokine pathways might be manipulated to enhance anti-tumour immunity and alleviate pathological inflammation in obesity. Such studies are conducted in collaboration with industry partners and international scientists.

Tumour burden and cancer patient outcomes are heavily affected by the level of immune cell infiltration in the primary tumour. Immune cell movement is controlled by a network known as the chemokine system that provides a roadmap and directs immune cells to sites of infection, wounds and malignancy in the body. Novel treatments that enhance T cell responses such as checkpoint inhibitors and CAR T cells are showing great promise and such targeted immunotherapies are expected to revolutionise cancer treatment. My work is focussed on identifying and assessing novel immunotherapies with a specific focus on those that can boost immune cell infiltration of tumours in patients with obesity-associated and inflammation-driven malignancy.

The worldwide obesity epidemic has been described as a global catastrophe in slow motion, with no country successfully curbing its escalation and prevalence tripling since 1975. The World Health Organisation estimates that 1.9 billion adults and 41 million children worldwide are overweight or obese and at great risk of developing obesity-associated disease such as diabetes, cancer or heart disease. Therefore, my research examines novel ways to treat and prevent these diseases, particularly the obesity-associated cancer oesophageal adenocarcinoma. Oesophageal adenocarcinoma (OAC) is an aggressive malignancy, with a dismal five year survival rate of only ~18%, mainly due to a poor treatment response rate of ~30%. Of all malignancies, OAC has one of the strongest associations with obesity and is one of the deadliest cancers placing it as one of the top 5 leading causes of cancer-related

deaths in males aged between 40 and 59. Worryingly, incidence rates have increased 38% in Ireland alone since the 1990s, with predicted increases of up to 160% in males by 2040. Therefore, novel treatments are urgently required to improve outcomes for the increasing number of patients with OAC, both nationally and globally.

Our recent published work has shown that T cells required for tumour eradication are recruited to the inflamed sites of visceral adipose tissue (VAT) and liver in OAC patients and we have identified the chemokine pathways responsible for this recruitment. The movement of T cells toward the VAT and liver away from the tumour poses a huge problem for launching effective anti-tumour immune responses. Furthermore, we have reported that natural killer (NK) cells migrate to the VAT and liver in OAC patients where their viability and functions are altered. We propose that such alterations in the frequencies and functions of these crucial anti-tumour immune cells is detrimental for anti-tumour immunity in OAC. The antibodies and reagents selected from the Immunotools panel will facilitate further profiling of natural killer cells and monocytes in OAC patients and contribute to the investigation of their role in obesity-associated inflammation and cancer. Furthermore, these reagents will allow us to examine the chemokines governing NK cell migration in these patients and provide insights into approaches to redirect NK cells toward tumour to enhance anti-tumour immunity in OAC.

At a time when the worsening obesity epidemic shows no signs of abating, our research examines how we might prevent and treat disease in the growing number of patients at huge risk of or who have already developed obesity-associated pathologies.

ImmunoTools *special* AWARD for **Melissa Conroy** includes 25 reagents

APC – conjugated anti-human CD3, CD19, CD24, CD56

FITC - conjugated anti-human CD11b, CD27, CD45, CD127, Annexin-V

PE - conjugated anti-human CD11b, CD14, CD16, CD27, CD56

PerCP - conjugated anti-human CD14

recombinant human cytokines: rh IFN-gamma, rh IL-1alpha, rh IL-2, rh IL-6, rh IL-10, rh ITAC, rh M-CSF, rh MIP-1 alpha, rh MIP-3 alpha, rh TNF-alpha

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