BCHM 421/422 Project – 2022-23

Project Outline

Supervisor: Dr Andrew Craig

Project Title: Developing a co-culture model for testing cancer immunotherapies targeting TGF-β and immune checkpoint inhibitors

Project Goals: The goals of this project are to:

1) Establish ovarian cancer cell lines with fluorescent reporter indicating release of Granzyme B from cytotoxic T cells

2) Test effects of TGF-β and immune checkpoint inhibitors on ovarian cancer cells co-cultured with cytotoxic T cells

Experimental Approaches:

1) Student will learn how to safely maintain sterile cultures of human ovarian cancer cell lines

2) Student will learn how to safely use lentiviruses encoding both chicken ovalbumin (OVA, a model tumour antigen) and a Forster resonance energy transfer (FRET) probe with a Granzyme B cleavage site between fluorophores (Ref 1.) to transduce and select ovarian cancer cell lines.

3) Student will learn how to isolate Ova-specific T cells from OT-1 transgenic mice.

4) Student will establish conditions for co-cultures with the above cell types in absence or presence of immune modulatory treatments (eg. TGF-β inhibitors and immune checkpoint inhibitors).

5) Student will learn how to use flow cytometry and confocal microscopy to measure the ability of T cells to kill cancer cells in the above culture models.

6) Student will learn about the potential for targeting of the TGF-β pathway can improve treatment options for ovarian cancer (Refs 2, 3).

References:

1. G Sharma, CM Rive and RA Holt (2019) Rapid selection and identification of functional CD8+ T cell epitopes from large peptide-coding libraries, Nature Communications, 10, 4553.

2. D Newsted et al. (2018) Blockade of TGF-β signaling with novel synthetic antibodies limits immune exclusion and improves chemotherapy response in metastatic ovarian cancer models, OncoImmunology 8(2):e1539613.

3. BM Roane, RC Arend and MJ Birrer (2019) Targeting the Transforming Growth Factor-Beta Pathway in Ovarian Cancer, Cancers 11(5), 10.3390