



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Investigating the function of tumour egressing CD8+ T cells in anti-tumour response	
Name	Dr Andrew On Wah Yam	
Award Received	2017 RACP Fellows Research Entry Scholarship	
Report Date	1 August 2018	
Chief Investigator / Supervisor	Dr Tatyana Chtanova	
Administering Institution	Garvan Institute of Medical Research	
Funding Period	Start Date:	1 March 2017
	Finish Date:	1 March 2018

PROJECT SUMMARY

Immune based therapies is one of the pillars for cancer treatment. There are currently several cancer immunotherapies that unlock immune cells known as T-cells to attack tumour cells. Unfortunately, this type of treatment is not always successful and is not effective for all cancers. One reason is that other immune cells, such as neutrophils, are protecting the tumour from being recognised by the immune system. Neutrophils are commonly found in cancers. They tend to be pro-tumour and work by suppressing the patient's immune system from recognising the tumour. Some cancer treatments have tried to overcome this issue by removing neutrophils but this has its downside of removing an important immune cell that is needed to fight bacterial infections. My research is looking at this problem from a different perspective. Instead of removing neutrophils from tumours, I am looking at recruiting anti-tumour neutrophils into tumours. To achieve this, I am injecting microbes into tumours to recruit anti-tumour neutrophils into the tumour. It is hoped that these stimulated neutrophils will reshape T cells in the tumour to fight cancer cells. So far my laboratory work has supported our hypothesis.

PROJECT AIMS / OBJECTIVES

Immunotherapy is one of the pillars to treat cancers. Some of the most exciting advances in immuno-oncology has been in T cell checkpoint inhibitors. Despite basic and clinical research advances in cancer immunotherapy, most patients do not have a durable response to treatment and it is not effective in all cancers. The reason that T cell checkpoint inhibitors are not entirely effective for all cancers and patients is that there are other immune cells within the tumour that supports an immunosuppressive environment and this includes the neutrophil. Neutrophils are present in nearly all tumours and are associated with a poor prognosis.

Existing cancer immunotherapies such as, checkpoint inhibitors, activate cytotoxic T cells but are only effective in a minority of patients and cancers. Clearly there is a clinical need to improve immunotherapeutic approaches to cancers. We hypothesize that harnessing anti-tumour function of neutrophils can reshape the tumour microenvironment leading to decreased tumour growth and providing an additional immune-based approach to treat cancers.

Hypothesis

Harnessing anti-tumour neutrophils within tumours will reshape the tumour microenvironment and promote decreased tumour growth by recruiting CD8+ T cells.

Overall Aim

To develop new immunotherapeutic approaches that would harness the power of neutrophils to provide a stronger more durable anti-tumour response.

Specific Aims

1. To reshape neutrophil function in tumours and to:
 - a. Identify the anti-tumour neutrophil phenotype
 - b. To investigate the effect of anti-tumour neutrophil on other immune cells subsets within the tumour microenvironment, particularly CD8+ T Cells
2. To investigate the role of neutrophil recruitment on tumour growth and its underlying mechanism
3. To investigate if the neutrophil anti-tumour response can improve the effect of checkpoint inhibitors

SIGNIFICANCE AND OUTCOMES

Neutrophils are an immune cell that are present in the majority of tumours. Their presence in tumours is associated with a poorer prognosis. Therefore, neutrophil depletion has been proposed a possible avenue to treat cancers, however this is limited by risks of immunosuppression. Our proposal takes a different approach and investigates whether activated anti-tumour neutrophils can be recruited into tumours are able to shape the adaptive immune system within the tumour microenvironment. Specifically, we have shown that neutrophil recruitment is associated with an activated T cell recruitment. This is associated with rapid reduction of tumour growth. Future experiments will investigate recruitment of activated T cell is neutrophil dependent and to clarify the T cell subtype recruited.

PUBLICATIONS / PRESENTATIONS

Oral Presentation

EMBL Australia Postgraduate Symposium 2017

Title: Developing Novel Innate-Based Approaches to Treating Cancer

Andrew O. Yam, Jacqueline Bailey, Tommaso Torcellan, Tatyana Chtanova

Poster Presentation

International Neutrophil Symposium 2018

Reshaping Neutrophil Function in Cancer

A.O. Yam, F. Lin, J. Bailey, J. Stolp, T. Chtanova.