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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		Cutaneous squamous cell carcinoma in immunocompetent and immunocompromised patients
Name		Dr Alesha Thai
Award Received		2019 Arnott Research Entry Scholarship
Report Date		May 2021
Chief Investigator / Supervisor		Prof Ben Solomon Prof Danny Rischin
Administering Institution		Peter MacCallum Cancer Centre
Funding Period	Start Date:	February 2019
	Finish Date:	February 2020

PROJECT SUMMARY

This research project has explored the immune microenvironment of both immunocompetent and immunocompromised patients with cutaneous s□uamous cell carcinoma (CSCC) to better understand the role of the immune system in the development and progression of this cancer.

CSCC is the second most common type of cancer diagnosed in Australia. The majority of patients are cured with surgery and/radiotherapy but a small subset of patients develops unresectable or metastatic disease. Immunotherapy has recently been shown in clinical trials to be very effective for patients with CSCC but is yet to be approved in Australia.

Patients with a low immune system (from drugs, or common blood cancers such as CLL) are at much higher risk of developing CSCC (over 100 fold risk) and their cancers are more lethal. However, they have been excluded from clinical trials and we have limited understanding on the differences in tumours that develop in patients with low immune systems compared to normal immune systems.

My project examined the CSCC tumor differences between immunocompromised and immunocompetent patients. I particularly focused on immune factors in and around the tumour as well as examining the genetic differences. Ultimately, my results, combined with others in the field may be able to identify potential pathways that can be targeted to prevent or better treat CSCC in immunocompromised patients.

PROJECT AIMS / OBJECTIVES

Aim 1: 1: Immunohistochemistry {IHC} to characterise the immune microenvironment of CSCC (n=180). We have analysed the tumoural location and abundance of immune cell subsets, including but not limited to CD8+ tumour infiltrating lymphocytes (TII s), CD4+ TII s, PD-LI+ immune cells {IC)

and tumour cells (TC} and CD103.

Aim 2: Comparisons in gene expression using the NanoString nCounter gene profiling platform will be used to compare the following groups:

a. Good and poor prognosis tumours

b. CSCC arising from immune competent vs. immunocompromised hosts

Aim 3: Compare the genomic differences (including tumour mutational burden and gene variants) between CSCC tumours arising in immunocompromised and immunocompetent patients.

SIGNIFICANCE AND OUTCOMES

To our knowledge, there has been limited research into the immune landscape of cutaneous squamous cell carcinomas (CSCC), particularly comparisons between immunocompetent and immunocompromised patients. CSCC has one of the highest tumour mutation burdens (TMB) in a recently tested cohort of 100,000 cancer cases. High TMB has been shown to be a sensitive predictor of response to immunotherapy. Whilst recent data have shown practice changing results in patients with CSCC receiving checkpoint blockade, we do not have an appreciation of the tumour immune microenvironment nor do we understand the lack of response in nearly half of patients with CSCC despite exceptionally high TMB.

Our project has shown unexpectedly, that there were no significant differences in CSCC tumours that develop in immunocompromised patients compared to immunocompetent patients with regards to the protein expression of key immune mediators such as PD-ll and CD103, or in genomic profiles. Based on our findings, we hypothesize that the aggressive and more lethal behaviour of CSCC in immunocompromised patients, are likely driven by host immune responses rather than differences in tumour biology.

Based on the work completed in this project, we are applying for funding to examine CSCC tumors in immunocompromised patients before and after treatment with immunotherapy to identify potential predictive biomarkers.

PUBLICATIONS / PRESENTATIONS

None thus far, but anticipated to have manuscript with all findings submitted for publication during Q4 of 2021.