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RACP Foundation Research Awards

FINAL REPORT

Project / Title		Investigating the immune landscape of end-stage high grade serous ovarian cancer
Name		Dr George Au-Yeung
Award Received		2018 RACP GlaxoSmithKline Research Establishment Fellowship
Report Date		30/01/2019
Chief Investigator / Supervisor		Professor David Sawtell
Administering Institution		Peter MacCallum Cancer Centre
Funding Period	Start Date:	17/12/17
	Finish Date:	18/12/18

PROJECT SUMMARY

High grade serous ovarian cancer is the most common epithelial ovarian cancer, and is responsible for the most deaths due to gynaecological cancers. Understanding the reasons for the development of treatment resistant disease will enable the design of novel clinical trials to improve patient survival.

This project aimed to characterise the immune landscape and gene expression profile of high grade serous ovarian cancer. We have selected 15 patients from the CASCADE rapid autopsy cohort to analyse and aim to characterise these samples to look for similarities and differences that may explain why these tumours grew and were resistant to treatment. Early analysis indicates significant degree of heterogeneity between tumour sites, indicating the potential challenges to personalised targeted therapies and the need for novel ways to assess heterogeneitv in patients in real-time.

PROJECT AIMS / OBJECTIVES

Aim 1: Correlation between immune cell infiltrate, genomic profile and gene expression

- Gene expression data has been generated from a pilot cohort of 15 patients, with up to 4 anatomical sites per patient. Via a collaboration with international investigators, proteomic data generated from these same sites are currently being analysed

Aim 2: Correlation between immune cell infiltrate and molecular subtype

- Multiplex immunohistochemistry analysis of matched samples will be undertaken and correlated with molecular subtype

Aim 3: Investigating temporal and spatial heterogeneity of molecular subtype

- Subtype switching has been proposed as a potential resistance mechanism. We propose to use gene expression data to characterise the subtype of HGSC patients at end-stage in multiple metastatic deposits, and compare this to the subtype at diagnosis.

SIGNIFICANCE AND OUTCOMES

The frequency of molecular subtypes at disease recurrence is unknown, as is the rate of subtype switching from primary to recurrent disease. The outcomes from this study will characterise the frequency of temporal and spatial heterogeneity, and inform the design of subtype specific clinical trials such as BEACON, a current trial open to target the C 1 molecular subtype.