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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		Mechanisms that facilitate metastatic potential in oral and base of tongue carcinomas
Name		Dr Annette Lim
Award Received		2016 RACP GlaxoSmithKline Research Establishment Fellowship
Report Date		25 October 2017
Chief Investigator / Supervisor		Dr Annette Lim
Administering Institution		Sir Charles Gairdner Hospital
Funding Period	Start Date:	1 January 2016
	Finish Date:	31 December 2016

PROJECT SUMMARY

The RACP-GSK grant has contributed to the extension of a larger three year project that investigates the role of nanovesicles, "cancer fragments", in the blood stream and the role of the immune system in oral cancers. Both are known molecular mechanisms that regulate the ability of cancer to spread.

The assessment of nanovesicles and their contents represents a liquid biopsy approach to cancer diagnosis and surveillance through isolation of these cancer fragments from body fluids. Liquid biopsies can also facilitate the personalisation of treatment for patients in the future through the examination of DNA and other molecules that exist on and within these cancer vesicles.

The role of the immune system is known to be a key regulator of cancer growth and spread in the body. Our research profiles the type of immune cells and immune signals in oral cancers in order to determine if particular immune patterns correlate with an increasing risk of developing advanced disease.

PROJECT AIMS / OBJECTIVES

AIM 1: We will assess the clinical significance of nanovesicles in circulating blood from a prospective cohort of OCSCC patients.

AIM 2: We will assess whether an impaired immune response contributes to the development of advanced disease.

SIGNIFICANCE AND OUTCOMES

Team growth, infrastructure and collaboration.

1) This project has helped established formal collaborations between the University of Western Australia, Sir Charles Gairdner hospital, the state pathology service- PathWest, St John of God Private Hospital, Hollywood Private Hospital and the Oral Health Centre of Western Australia.

2) We have hired a new research assistant given the resignation of the previous (Feb 2017), after having more than 150 applicants for the position.

3) We have had 2 honours students join the research team and one Cancer Council WA vacation scholarship student completed his work experience with us Feb 2017. A final year medical oncology advanced trainee has successfully received a WA health grant to do a one year fellowship in the laboratory with us on this project and is currently involved in patient recruitment.

4) With PathWest, we have designed a customised DNA mutation next generation sequencing panel specific for head and neck cancer which represents one of few of its kind. The collaboration with PathWest is aimed to promote rapid translation of results into clinical practice.

5) We have been able to springboard our research to develop other collaborative projects with other cancer streams and other universities (Edith Cowan University) to investigate liquid biopsy technology in other biofluids.

6) We have submitted four further grant applications to secure additional funding to further develop this translational research program and have recently been awarded on further Department of health WA Merit Award for continuation of this work.

7) We have obtained a new instrument with additional support from philanthropic donations for a qNano machine that has improved the efficiency of methodology of TEX sample analysis.

8) We have secured formal collaboration with the Institute of Health Research (The University of Notre Dame, Fremantle) for statistical analyses.

Laboratory analyses.

AIM 1: 1) We are readily able to identify nanovesicles from blood samples with transmission electron microscopy confirming the expected size range of particles between 50-200nm (median 139nm). Quantification of extracted nanovesicles with qNano demonstrated a median of 4.87x109 nanovesicles/mL being isolated from samples. Common known mutations in head and neck cancer and targetable mutations have been identified in both tumour tissue and nanovesicles including mutations in TP53, PI3K, and CDKN2A. Ongoing analyses and validation are being performed to assess similarities and differences between samples from participants from varying disease stages and following treatment.

AIM 2: Immunohistochemical analyses are near complete and are under review by expert head and neck pathologists who will report on both the nature of the immune infiltrate and the location with respect to the tumour. Other novel immune profiling analyses are near complete ready for data analyse

PUBLICATIONS / PRESENTATIONS

This study is ongoing as it forms a part of a larger 3 year project.