

AWARD NUMBER: HT9425-23-1-0099

TITLE: Investigating the Role of Nitric Oxide in the Immune Regulation of Non-Small Cell Lung Cancer

PRINCIPAL INVESTIGATOR: Marie-Liesse Asselin-Labat

CONTRACTING ORGANIZATION: The Walter and Eliza Hall Institute of Medical Research
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REPORT DATE: March 2024

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE		<i>Form Approved</i> <i>OMB No. 0704-0188</i>	
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1. REPORT DATE March 2024	2. REPORT TYPE Annual	3. DATES COVERED 15 Feb 2023 – 14 Feb 2024	
4. TITLE AND SUBTITLE Investigating the Role of Nitric Oxide in the Immune Regulation of Non-Small Cell Lung Cancer		5a. CONTRACT NUMBER	
		5b. GRANT NUMBER HT9425-23-1-0099	
		5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Marie-Liesse Asselin-Labat Anthony Purcell E-Mail: labat@wehi.edu.au		5d. PROJECT NUMBER	
		5e. TASK NUMBER	
		5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Walter Eliza Hall Institute 1G Royal Parade, Vic, 3052 Australia		8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012		10. SPONSOR/MONITOR'S ACRONYM(S)	
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			
13. SUPPLEMENTARY NOTES			
14. ABSTRACT A main contributor to respiratory diseases is the constant exposure to air pollutants during the deployment of military personnel. During operations, military personnel are exposed to multiple factors external to the conflict, including air contaminants and pollutants that affected their health. Most military personnel have reported acute respiratory effects due to exposure to air contaminants. The main sources of air pollutants are diesel exhaust, sandstorms, firearms fumes and smoke from burn pits. Studies have shown these pollutants highly contribute to lung pathologies among military personnel, increasing the prevalence of lung inflammatory diseases. Burn pit smoke is considered the major source of air pollution in the field. Studies have shown the correlation between exposure to burn pit smoke and cancer development. Inhalation of combustion fumes alters the expression of different metabolic enzymes, including nitric oxide synthases (NOS1, NOS2, NOS3). In healthy tissues, NOS isoforms modulate an array of cell transduction signals that control tissue vascularization, immune regulations and tissue repair. Deregulation of the balance of expression of the different isoforms increases the production of nitric oxide in cells, altering nitration and nitrosylation of proteins. These post-translational modifications of proteins have been associated with lung inflammatory disease and alteration of the immune response. Specifically, overexpression of NOS2 and NOS3 is associated with worst prognosis in lung adenocarcinoma. Our proposal addresses the role of the different NOS isoforms in regulating the visibility of tumor cells to the immune system and how they participate in the remodeling of the tumor microenvironment, addressing an issue of huge importance to military personnel exposed to combustion fumes. In our analysis of lung adenocarcinoma, we have found that the type of immune infiltration (myeloid or lymphoid) was predictive of patient outcome. However in this cohort, expression of NOS2 or NOS3 did not appear to be associated with survival. We now will evaluate how nitrosylation of neoantigens may affect the immune infiltrate and the type of immune response that may be associated with prolonged survival.			
15. SUBJECT TERMS None listed.			
16. SECURITY CLASSIFICATION OF:		17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES
			19a. NAME OF RESPONSIBLE PERSON USAMRDC

a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	UU	20	19b. TELEPHONE NUMBER <i>(include area code)</i>
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Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. Introduction

LUAD is the most prevalent subtype of lung cancer. Tumor cells acquire numerous molecular changes to support their proliferation and survival. Some alterations result in the expression of neoantigens by tumor cells, neoantigens form from proteins processed in the immunoproteasome before being presented to the immune system by the major histocompatibility complex (MHC-I/II). Little is known about how post-translational modifications (PTM) induced in cancer cells by diverse metabolic pathways affect the processing, presentation and immunogenicity of neoantigens. In this proposal, we will evaluate the effect of protein nitrosylation and nitration on tumor immunogenicity and its effect on the remodeling of the tumor microenvironment.

The inducible nitric oxide synthase (iNOS) pathway generates nitric oxide, a free radical species, activating multiple downstream transduction signals, including PTM of proteins by nitration of tyrosine or nitrosylation of cysteine residues. Nitrosylation of tyrosine in the tumor suppressor protein TP53, has been shown to regulate TP53 oligomerization resulting in deregulation of the cell cycle. Nitration of tyrosine residues has also been linked to autoimmune diseases where 3-nitrotyrosine peptides are recognized as non-self by the immune system, demonstrating the **importance of NOS/NO-mediated PTM on peptide immunogenicity**. We aim to evaluate the effect of nitrosylation on the transcriptome of tumour cells and how nitrosylated peptides may play a role in regulating immune infiltration and immune response.

2. Keywords

Tumor neoantigens, post-translational modifications, nitrosylation

3. Accomplishments

What were the major goals of the project?

Major Task 1: Correlate the immune profile with iNOS/eNOS expression

Due 02/01/2024 – 100% complete

Major Task 2: Identify pathways affected by nitrosylation that may modulate immune cells recruitment in a tumor Due

11/30/2024 – 50% complete

Major Task 3: Effect of nitration/nitrosylation on the immunopeptidome

Due 02/01/2024 – not started

What was accomplished under these goals?

Major Task 1: Correlate the immune profile with iNOS/eNOS expression

We received approval from DOD OHRO for the use of HAS.

We perform Multiplex Immuno-Histochemistry of patient samples with the MIBIScope that uses ion-beam ablation and time-of-flight MS. Samples are part of a repository of 108 lung adenocarcinoma (LUAD) de-identified FFPE samples obtained from the Victorian Cancer Biobank

Outcome: Deep profiling of the immune microenvironment and unsupervised clustering of samples resulted in the stratification of patients into 3 subgroups in LUAD. Most tumors had high lymphoid infiltration rich in T and B cells (84%) either alone (48%) or mixed with myeloid cell infiltration (LM-enriched, 36%). Myeloid-enriched tumors only represented 15% of the LUAD samples. Staining for iNOS and eNOS showed eNOS/iNOS-positive tumours in all 3 groups, irrespective of the immune infiltrations. Correlation of the immune profiling with patients outcomes revealed that Myeloid-enriched tumours had worse outcome, irrespective of iNOS/eNOS expression. iNOS/eNOS expression was not associated with patient outcomes in lymphoid tumours.

Major Task 2: Identify pathways affected by nitrosylation that may modulate immune cells recruitment in a tumor Due

11/30/2024 – 50% complete

In this goal, we planned to perform total proteome analysis of NOS inhibitor treated cells and identify signaling pathways altered by NOS inhibition.

These tasks relied on choosing the right cell line and the right culture conditions with inhibitors to perform proteomic by LC-MS/MS and transcriptomic analyses. Unfortunately, one of the cell lines proposed in the SOW, H2077, did not respond to stimulation with Nitric oxide donors. We also had to adjust the treatment protocol with serum-starvation of the cells to better detect nitrosylation signals. We have now identified the right cell lines (H23 and H1975) and the right culture conditions to induce/inhibit nitrosylation, and are ready to take on the next step of the project for major tasks 2 and 3.

What opportunities for training and professional development has the project provided?

Post-doctoral fellow (Alejandro Torres) had the opportunity to develop his data analysis skills and took an 'Introduction to R course (a free course for post-doctoral fellows) run by the Institute for biologists. He also participated and presented his work at the Lorne Cancer Conference in 2023.

How were the results disseminated to communities of interest?

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period to accomplish the goals and objectives we will complete major Task 2 with he proteomic and transcriptomic analysis. We will also complete Major Task 3 with the immunopeptidomic analysis.

4. Impact

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. Changes/Problems

Changes in approach and reasons for change

One of the cell lines proposed in the SOW, H2077, did not respond to stimulation with Nitric oxide donors. We have now identified the right cell lines (H23 and H1975) to use and can complete the project.

Actual or anticipated problems or delays and actions or plans to resolve them

We do not anticipate further delays than the ones encountered in year 1.

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. Products

Conference papers, and presentations.

Poster presentation at Lorne Cancer Conference, February 2023, Lorne Australia:

Discovering Neo-antigens: Variability in the immunopeptidome of Non-Small Cell Lung Cancer patients.

Alejandro Torres-Riquelme, Dan Batey Kirti Pandey, Kate Scull, Anthony Purcell, and Marie-Liesse Asselin-Labat.

7. Participants & Other Collaborating Organizations

Name:	Alejandro Torres-Riquelme
Project Role:	<i>Post-graduate Fellow</i>
Researcher Identifier (e.g. ORCID ID):	NA
Nearest person month worked:	6
Contribution to Project:	<i>Mr. Torres-Riquelme has performed work for multiplex immunostaining data generation and analysis in Major Task 1 and cell line work for Major Task 2.</i>
Funding Support:	DoD Concept Award

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Yes, see appendices

What other organizations were involved as partners?

Nothing to report. The work at Monash University will start in year 2 of the grant

8. Special Reporting Requirements

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from **BOTH** the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ebrap.org> for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on <https://usamraa.health.mil>) should be updated and submitted with attachments.*

9. Appendices

Other Support Asselin-Labat

Other Support Anthony Purcell

Support
Pending

Title	IMMUNE CONTROL OF CANCER: INCREASING TUMOUR CELL VISIBILITY
Time commitments	This fellowship will cover my salary for the performance period.
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	NHMRC Investigator Grant/Cancer Australia Grant National Health and Medical Research Council (NHMRC) Email: help@nhmrc.gov.au Postal address: National Health and Medical Research Council GPO Box 1421 Canberra ACT 2601 Australia
Performance period	2024 - 2028
Level of funding	
Brief description of the project's goals	Fellowship application to support PI Asselin-Labat's salary for a comprehensive research program to increase tumor cell visibility and anti-tumor immunity on lung cancer
List of the specific aims	<ol style="list-style-type: none"> 1. Augment the presentation of neoantigens 2. Increase immunity against neoantigens 3. Engage an active immune milieu
Does the proposed project overlap with this funding?	There is a partial overlap between Aim 1 of this NHMRC application and Aim 2 of the proposed research. However, there is no duplication of funds as the NHMRC funds will be used for my salary support whereas the funds request from DoD LCRP will be used for the consumables cost and the salaries of the post-doctoral fellows executing the work.

Title	Identifying and overcoming mechanisms of immune evasion in cancer
Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	NHMRC Synergy Grant/Cancer Australia Grant National Health and Medical Research Council (NHMRC) Email: help@nhmrc.gov.au Postal address: National Health and Medical Research Council GPO Box 1421 Canberra ACT 2601 Australia
Performance period	2025 - 2029
Level of funding	
Brief description of the project's goals	To identify key cellular interactions and molecular pathways that determine outcomes of anti-cancer immunity and to develop novel cancer therapies.
List of the specific aims	<ol style="list-style-type: none"> 1. Identifying novel tumour cell-intrinsic factors regulating immune evasion 2. Understanding CD8 T cell function and dysfunction in tumour control and response to immunotherapy 3. Investigating pro- and anti-tumour functions of CD4 T cells

	4. Evaluating combination therapy with immune checkpoint blockade
Does the proposed project overlap with this funding?	There is no overlap.

Title	The Australian Clinical Centre for Emerging Spatial Science
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	Medical Research Future Fund - National Critical Infrastructure Grant National Health and Medical Research Council (NHMRC) Email: help@nhmrc.gov.au Postal address: National Health and Medical Research Council GPO Box 1421 Canberra ACT 2601 Australia
Performance period	May 01, 2023- Apr 31, 2028
Level of funding	
Brief description of the project's goals	To facilitate access to cutting-edge spatial technologies for clinicians and clinician-scientists Australia-wide, through the development of an infrastructure that will bring state-of-the-art -omics technologies currently to anatomical pathology.
List of the specific aims	<ol style="list-style-type: none"> 1. Develop a pipeline that integrates spatial omic data with clinical data in the tissue biopsies that are routinely obtained to diagnose chronic inflammatory and autoimmune diseases 2. Explore and compare target organ pathology in molecular detail to improve understanding of pathogenesis and prognosis, and to discover better biomarkers 3. Facilitate personalised medicine and selection of the most appropriate therapies based on end organ pathology, and rationalise patient selection for clinical trials
Does the proposed project overlap with this funding?	There is no overlap.

Current

Title	Investigating the Role of Nitric Oxide in the Immune Regulation of Non-Small Cell Lung Cancer
Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	US Department of Defense Grant US Department of Defense <i>Science Officer Assignment:</i> <i>Michael Hall michael.d.hall14.civ@health.mil</i>
Performance period	Feb 15, 2023- Feb 14, 2024
Level of funding	
Brief description of the project's goals	To identify spliced neo-antigens in lung adenocarcinoma
List of the specific aims	<ol style="list-style-type: none"> 1. Perform deep profiling of the immune microenvironment of iNOS^{hi} and iNOS^{lo} LUAD

	<ol style="list-style-type: none"> 2. Elucidate the downstream pathways affected by protein nitration/nitrosylation in LUAD 3. Determine the effect of nitration/nitrosylation on the immunopeptidome
Does the proposed project overlap with this funding?	There is no overlap.

Title	Targeting the immunopeptidome of non-small cell lung cancer as a new therapeutic approach
Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	<p>Cancer Council Victoria Grant CancerCouncilGrants@cancervic.org.au</p> <p>615 St Kilda Rd, Melbourne Vic 3004 Australia</p>
Performance period	Jan 01, 2023-Dec 31, 2024
Level of funding	
Brief description of the project's goals	To identify spliced neo-antigens in lung adenocarcinoma
List of the specific aims	<ol style="list-style-type: none"> 1. To evaluate the activity of the immunoproteasome in lung adenocarcinoma 2. To identify immunogenic spliced neoantigens in lung adenocarcinoma 3. To evaluate the presence of recurring immunogenic spliced-neoantigens across patients
Does the proposed project overlap with this funding?	There is no overlap.

Title	Spatial multi-omic analysis to evaluate the effect of immune pressure on tumor immune escape mechanisms
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	<p>Melbourne Academic Centre for Health mach-admin@unimelb.edu.au</p> <p>Location: Level 2, 21 Bedford Street, North Melbourne, 3051 Australia</p>
Performance period	July 01, 2021-Dec 31, 2022
Level of funding	
Brief description of the project's goals	To integrate spatial proteomic and transcriptomic to understand immune escape mechanisms in NSCLC
List of the specific aims	<ol style="list-style-type: none"> 1. Determine intra- and inter- tumor heterogeneity in the transcriptome of NSCLC 2. Profile in-depth immune cells in NSCLC 3. Integrate tumor and immune cell profiles to decipher tumor evolution and immune escape
Does the proposed project overlap with this funding?	There is no overlap.

Title	Elucidating differences in lung cancer formation in smoker and never smoker lung cancer
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Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	Perpetual Trustees Impact Grant, Harry Secomb Trust Perpetual Trustees Emily Wellard-Baring Senior Philanthropy & Non Profit Services Manager Perpetual GPO Box 4172 SYDNEY NSW 2001 Australia Email: philanthropy@perpetual.com.au
Performance period	June 01, 2020- May 31, 2023
Level of funding	
Brief description of the project's goals	To study how the immune cells in the vicinity of lung tumor cells drive tumor evolution in never-smoker and smoker lung cancer.
List of the specific aims	<ol style="list-style-type: none"> 1. To develop preclinical models to interrogate the interactions between immune cells and tumor cells 2. To characterise the composition and activation status of tumor-infiltrating immune cells in never smoker and smoker lung cancer 3. To test response to inhibitors of T-cell co-inhibitory molecules and/or agonists of T-cell co-stimulatory molecules in never smoker and smoker lung cancers
Does the proposed project overlap with this funding?	There is no overlap.

Title	Effect of DNA damaging agents on the lung immune microenvironment and the initiation of lung cancer
Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	NHMRC Ideas Grant National Health and Medical Research Council (NHMRC) Email: help@nhmrc.gov.au Postal address: National Health and Medical Research Council GPO Box 1421 Canberra ACT 2601 Australia
Performance period	Jan 01, 2020- Dec 31, 2023
Level of funding	
Brief description of the project's goals	To decipher the impact of DNA damaging agents on both the epithelial and T-cell compartment in the lung to determine how these molecular damages and repair processes shape NSCLC tumor growth
List of the specific aims	<ol style="list-style-type: none"> 1. Define molecular events regulating lung epithelial cell response to DNA damage 2. Determine the effect of exposure to DNA damaging agents on lung resident T-cells 3. Decipher how resident T-cells and genomic instability shape lung cancer development
Does the proposed project overlap with this funding?	There is no overlap.

Title	Evaluating direct and indirect effects of SARS-CoV2 on multiple organ systems using stem cell-derived human tissues
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	Victoria DHHS COVID Research Fund Department of Health and Human Services Office of Health and Medical Research – The Department of Health and Human Services Office of Health and Medical Research 50 Lonsdale Street, Melbourne, VIC 3000 Email: OHMR@dhhs.vic.gov.au
Performance period	Oct 01, 2020- June 30, 2023
Level of funding	
Brief description of the project's goals	To understand whether the clinical presentation after infection with SARS-CoV2 is the result of the specific effect of the virus on distinct organs or whether the damage is the result of the inflammatory response to the virus
List of the specific aims	<ol style="list-style-type: none"> 1. Evaluating the effect of SARS-CoV-2 on lung epithelial cells 2. Identifying underlying genetic risk factors and mode of action of COVID-19-related cardiomyopathy 3. Evaluating the effect of ACE inhibitors on SARS-CoV-2 response in the kidney 4. Modelling the neuroinvasive potential of SARS-CoV2 and relevance to clinical outcomes 5. Modelling the interaction between macrophages and endothelium to study the pathology of COVID-19
Does the proposed project overlap with this funding?	There is no overlap.

Title	Regulation of lung stem cells in development and disease
Time commitments	This fellowship covers my salary for the performance period.
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	Viertel Foundation Senior Medical Researcher Fellowship The Viertel Charitable Foundation The Viertel Charitable Foundation, C/O-Equity Trustees charities@eqt.com.au
Performance period	Jan 01, 2016- Oct 01, 2023 (on hold Oct 2016- June 2019)
Level of funding	
Brief description of the project's goals	To identify factors regulating lung stem cells at specific stages of lung morphogenesis, to elucidate key regulators involved in the repair of the diseased lung.
List of the specific aims	<ol style="list-style-type: none"> 1. Identify novel epigenetic regulators of embryonic mouse lung progenitor cells 2. Evaluate the role of long non-coding RNAs in mouse lung progenitor cells 3. Identify growth factors regulating mouse and human adult lung stem cells 4. Evaluate stem cells as the cells of origin of lung cancer
Does the proposed project overlap with this funding?	There is no overlap.

Previous

Title	Assessing the repurposing of clinical compounds in lung organoids as an alternative to the use of animal models for treatment of COVID-19 infection
Time commitments	2%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	MAWA Trust Research Grant The MAWA Trust The MAWA Trust Email : info@mawa-trust.org.au
Performance period	June 2020 – Dec 2020
Level of funding	
Brief description of the project's goals	To rapidly screen ~30 safe and well-tolerated drugs and compounds so they could be rapidly scaled for widespread use if found to be effective against COVID-19.
List of the specific aims	<ol style="list-style-type: none"> 1. Evaluate VitroGel as a replacement for Matrigel in the culture of lung organoids 2. Measure efficacy of selected drugs on SARS-CoV-2 virus replication and cell survival 3. Determine mechanisms of action of active compounds in lung cells
Does the proposed project overlap with this funding?	There is no overlap.

Title	ACRF program for resolving cancer complexity and therapeutic resistance
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	Australian Cancer Research Foundation – Equipment Grant Australian Cancer Research Foundation Kerry Strydom, CEO Australian Cancer Research Foundation, Suite 903, 50 Margaret Street, Sydney NSW 2000 Australia E-mail: kstrydom@acrf.com.au
Performance period	2020
Level of funding	
Brief description of the project's goals	Equipment grant to acquire novel imaging and transcriptomic technologies to evaluate therapeutic resistance at the single cell level.
List of the specific aims	<ol style="list-style-type: none"> 1. Link genotype and the epigenetic landscape with phenotype and cancer biology at the single cell level and define how these relationships change with disease development and treatment (diagnosis, relapse, metastasis etc) 2. Define in situ the relationships between cancer cells and immune and other cells within the cancer microenvironment at single cell resolution and how these change with, and influence, cancer treatment 3. Define the genetic and epigenetic drivers of cancer clonal evolution and resistance to therapy at the single cell level 4. Develop innovative computational biology and bioinformatic

	approaches to model and reconstruct cancer cell behaviour and treatment response at single cell resolution including integration of data sets across the Program
Does the proposed project overlap with this funding?	There is no overlap.

Title	Identification of cancer circulating cells in the peripheral blood of low-dose CT scan individuals at high risk of developing lung cancer
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	CEDAR Knight Cancer Institute Project Grant CEDAR Knight Cancer Institute Becky Reddaway reddaway@ohsu.edu 3181 S.W. Sam Jackson Park Road Portland, OR 97239-3098
Performance period	Jan 2018-July 2019
Level of funding	
Brief description of the project's goals	To investigate the characteristics of a rare population of hybrid cells present in the tumor and the circulation in lung cancer patients and define its role as a potential marker of progressive disease.
List of the specific aims	1. Determine the origin of hybrid cells in NSCLC 2. Define the molecular and functional differences between THC, NHC and CHC 3. Determine if the presence of THC is a predictor of patient outcome
Does the proposed project overlap with this funding?	There is no overlap.

Title	Germline mutation in DNA damage repair genes as a predictor of lung cancer risk in heavy smoker
Time commitments	10%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	CEDAR Knight Cancer Institute Project CEDAR Knight Cancer Institute Becky Reddaway reddaway@ohsu.edu 3181 S.W. Sam Jackson Park Road Portland, OR 97239-3098
Performance period	Jan 2018- Dec 2018
Level of funding	
Brief description of the project's goals	To determine if there is an interaction between germline mutations in DNA repair genes and exposure to tobacco that accelerate the onset of lung cancer in smokers.
List of the specific aims	1. Use computational biology approaches to compare the frequency of germline mutations in DNA repair genes in lung cancer patients with smoking history and a general healthy population 2. Perform targeted sequencing of a subset of DNA repair genes in smokers with or without lung cancer
Does the proposed project overlap with this funding?	There is no overlap.

Title	Immune profiling of lung carcinoma in situ
Time commitments	5%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	CEDAR Knight Cancer Institute Grant-in-Aid CEDAR Knight Cancer Institute Becky Reddaway reddaway@ohsu.edu 3181 S.W. Sam Jackson Park Road Portland, OR 97239-3098
Performance period	Jan 2018- Dec 2018
Level of funding	
Brief description of the project's goals	To identify differences in the immune signature of regressive and progressive lung carcinoma in situ
List of the specific aims	Perform Nanostring GeoMx on lung carcinoma in situ samples and compare the immune profile of regressive and progressive lesions.
Does the proposed project overlap with this funding?	There is no overlap.

Title	Identification of epigenetic regulators of lung development.
Time commitments	15%
Supporting agency name and address of the funding agency's procuring Contracting/Grants Officer	NHMRC Project Grant National Health and Medical Research Council (NHMRC) Email: help@nhmrc.gov.au Postal address: National Health and Medical Research Council GPO Box 1421 Canberra ACT 2601 Australia
Performance period	Jan 2015- Dec 2017
Level of funding	
Brief description of the project's goals	Understand how the epigenetic machinery mediates the transcriptional and structural changes required for embryonic lung formation to understand the development of lung diseases
List of the specific aims	1. Perform screens to identify novel epigenetic regulators of lung development 2. Evaluate the role of Ezh2 in embryonic lung development 3. Identify long non-coding RNAs which regulate lung development
Does the proposed project overlap with this funding?	There is no overlap.

**PHS OTHER SUPPORT
For All Application Types – DO NOT SUBMIT UNLESS REQUESTED**

There is no "form page" for reporting Other Support. Information on Other Support should be provided in the format shown below.

*Name of Individual: **Purcell, Anthony**
Commons ID: TPURCELL

Other Support – Project/Proposal

ACTIVE

Title: The "dark immunopeptidome" as a source of CD8 T cell epitopes in type 1 diabetes
Major Goals: This collaborative NIH RO1 grant aims to understand T cell selection and novel targets of T cell mediated pathology in celiac disease.

Status of Support: Active

Project Number: 1R01DK135079-01

Name of PD/PI: DiLorenzo, Teresa

Source of Support: NIH

Primary Place of Performance: Einstein College of Medicine, NY, USA

Project/Proposal Start and End Date: 01/01/2023-12/31/2024

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2023	2.40 calendar
2. 2024	2.40 calendar

Title: Shining a light on bat cellular immunity following virus infection

Major Goals: The major goals of this project are to develop reagents and methods to study cell mediated immunity in bats.

Status of Support: Active

Project Number: 1R21AI169481-01

Name of PD/PI: Baker, Michelle

Source of Support: NIH via CSIRO

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 05/01/2022-04/30/2024

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
2. 2022	1.20 calendar
3. 2023	0.60 calendar

Name of Individual: Purcell, A
Commons ID: TPURCELL

Title: Dominant classes of tumour specific antigens in Melanoma

Major Goals: The goal of this study is to identify and characterise the mechanism of generation of Melanoma specific antigens and their peptide epitopes.

Status of Support: Active

Project Number: APP2013631

Name of PD/PI: Purcell, Anthony

Source of Support: National Health and Medical Research Council (Australian Government) [NHMRC, equivalent to NIH system of grants]

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 01/01/2022-12/31/2024

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	1.2 calendar
2. 2023	1.2 calendar
3. 2024	1.2 calendar

Title: An investigation into T cell immunity towards metabolites

Major Goals: This project aims to investigate how the immune system responds to small molecule metabolites.

Status of Support: Active

Project Number: DP220102401

Name of PD/PI: Rossjohn, Jamie

Source of Support: Australian Research Council

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 01/2022-12/2024

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	1.2 calendar
2. 2023	1.2 calendar
3. 2024	1.2 calendar

Name of Individual: Purcell, A
Commons ID: TPURCELL

Title: An integrated approach to antigen discovery in autoimmunity and cancer

Major Goals: This Investigator grant includes support for my salary and research support to continue my program of antigen discovery in cancer and autoimmunity.

Status of Support: awarded

Project Number: APP2016596

Name of PD/PI: Purcell, Anthony

Source of Support: Australian National Health and Medical Research Council

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 01/01/2023-12/31/2027

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2023	Salary Support
2. 2024	Salary Support
3. 2025	Salary Support
4. 2026	Salary Support
5. 2027	Salary Support

Title: Targeting the immunopeptidome of non-small cell lung cancer as a new therapeutic approach

Major Goals: This grant includes examines non-canonical antigen presentation in lung adenocarcinoma.

Status of Support: awarded

Project Number: VG2022

Name of PD/PI: Asselin-Labat

Source of Support: Cancer Council of Victoria Venture Grant

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 01/01/2023-12/31/2024

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2023	0.6 calendar
2. 2024	0.6 calendar

Name of Individual: Purcell, A
Commons ID: TPURCELL

Pending Research Proposals

Title: Determining the impact of gluten-reactive T cell responses and environmental triggers on sensitivity to gluten and persistent enteropathy in Celiac Disease

Major Goals: This NIH R01 grant investigates T cell responses to dietary antigens and their role in the pathology of celiac disease.

Status of Support: Under funding consideration

Project Number:

Name of PD/PI: Purcell, Anthony

Source of Support: Australian National Health and Medical Research Council

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 06/01/2024-05/31/2029

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2024	1.2 calendar
2. 2025	2.4 calendar
3. 2026	2.4 calendar
4. 2027	2.4 calendar
5. 2028	2.4 calendar
6. 2029	1.2 calendar

Title: Next generation treatments in psoriasis: Restoring systemic and dermatological antigen-specific self-tolerance in the susceptible HLA-C*06:02+ patient cohort

Major Goals: This grant aims to develop immune tolerizing strategies to target HLA-C*06:02 restricted immune responses in psoriasis.

Status of Support: Under funding consideration

Project Number:

Name of PD/PI: Braun, Asolina

Source of Support: NIBR Global Scholars Program

Primary Place of Performance: Monash University

Project/Proposal Start and End Date: 01/01/2024-12/31/2026

Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2024	0.6 calendar
2. 2025	0.6 calendar
3. 2026	0.6 calendar

Name of Individual: Purcell, A
Commons ID: TPURCELL

IN-KIND

Name of CI: Purcell, Anthony
Source of Support: Monash University
Total In-Kind contributions:

***Overlap** (summarized for each individual):

There is no overlap with the active or pending projects and activities, other positions, affiliations, and resources and this application in terms of the science, budget, or an individual's committed effort

I, Anthony Purcell, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

*Signature:  _____

Date: 03/09/2024