Expediting Lung Cancer Diagnosis and Understanding Immune Dysregulation in Never and Former Smoking Patients

Principal Investigator: Julia Naso
Co-Investigators: Emilia Lim, Mark Trinder, Anna McGuire, Will Lockwood

Dear Lung Cancer Canada and GOMRG Committee:

We are pleased to submit our project 'Expediting Lung Cancer Diagnosis and Understanding Immune Dysregulation in Never and Former Smoking Patients' for the Geoffrey Ogram Memorial Research Grant.

A minimally invasive technique for promptly distinguishing whether pulmonary nodules are benign or malignant is critical for achieving earlier diagnosis of lung cancer. This need is heightened among never smokers, who are currently not eligible for screening programs and therefore at particular risk of delayed diagnosis. In the setting of equivocal imaging findings, receiving a non-diagnostic biopsy result or use of a 'watch and wait' approach extends uncertainty about the diagnosis, with significant impacts on patient anxiety and quality of life.

This project aims to leverage differences in the immune microenvironments of lungs with vs. without cancer to shorten time to diagnosis. We propose to (i) develop a clinically translatable test that can enable earlier and safer lung cancer diagnosis through profiling of the immune cells present in routinely collected minimally invasive clinical specimens that would otherwise be nondiagnostic for malignancy and (ii) characterize unique features of the lung immune microenvironments in never vs. former smoking patients, generating insights of potential relevance to both prevention strategies and immune modulatory treatments for the never smoking population.

Thank you for reviewing our application and for your support of lung cancer research. We look forward to pursuing our project's potential for sustained and powerful impacts on patient care.

Sincerely,

Julia Naso
Consultant Thoracic Pathologist, Vancouver General Hospital
Clinical Assistant Professor, Pathology and Laboratory Medicine, University of British Columbia

Summary of Proposed Research:

Pulmonary nodules detected incidentally or on screening may be benign or malignant, and diagnostic tools for promptly distinguishing these possibilities are critical for patient care. Benign and malignant nodules can be indistinguishable on imaging, with radiologic follow-up over multiple years required for exclusion of malignancy in the absence of a tissue diagnosis. Bronchoalveolar lavage is a common minimally invasive procedure that collects airspace cells from a region of lung for diagnostic evaluation (~900 procedures/year at our site). Microscopic examination of BAL specimens can only diagnose malignancy when the malignant cells are captured, resulting in false negative results in ~80% of truly malignant cases.[1,2] **Without a diagnosis it is challenging to optimize patient care, in some cases leading to unnecessary or delayed surgical interventions**. The problem of indeterminate pulmonary nodules is expected to grow as increased CT screening results in the detection of more nodules.

Never-smoking patients are in particular need of advancements in early lung cancer diagnosis, as they are currently not eligible for screening programs. Genomic landscapes of lung cancer in never smoking patients have shown intriguing differences from smoking-associated cancers,[8,9] and we hypothesize that the lung cancer immune microenvironment may differ in never vs former smokers. Mechanisms of lung cancer development in patients are poorly understood, with possible central roles for altered immune cell activity[4–6] including IL-1β dysregulation[7] (Fig. 1). Characterizing these differences is key to developing effective prevention and management strategies for the never-smoking population.

We propose that the non-neoplastic cells in bronchoalveolar lavage specimens that would otherwise be reported as negative may be leveraged to (i) inform on a patient's risk of malignancy and (ii) provide insight into unique immune microenvironment features in never vs. former smokers. Lung cancer is known to alter gene expression in local macrophages, driving pro-tumorigenic and immunosuppressive shifts in the immune microenvironment.[10–13] Advanced lung cancer has been associated with altered immune cell gene expression patterns compared to healthy controls, using bronchoalveolar lavage specimens (AUC=0.92).[14,15] However, these findings have not yet been translated to standard formalin-fixed paraffin embedded (FFPE) clinical specimens, to early-stage lung cancer patients, or to distinction from benign nodules, all factors key to achieving clinical utility for a lung cancer risk prediction test.

The present study **aims to characterize immune-related gene expression signatures in non-neoplastic cells surrounding benign and malignant pulmonary nodules, using archival clinical bronchoalveolar lavage specimens**. Specific aims are to identify differences in gene expression between specimens from:

1. Patients with vs without lung adenocarcinoma (including never and former smokers, Aim 1).
2. Never-smoking patients with vs without lung adenocarcinoma (Aim 2).
3. Patients with lung adenocarcinoma who have never vs formerly smoked (Aim 3).

Results of Aim 1 will be used to identify a signature predictive of malignancy, with the potential to be readily translated into a cost-effective test (~$150/sample) on clinical bronchoalveolar specimens that could be run as part our accredited hospital laboratory's weekly NanoString assay runs. Depending on the sensitivity and specificity, this test could be useful for diagnostic confirmation or helping patients with extremely low risk of cancer avoid further diagnostic procedures or unnecessary surgery. The immune microenvironment changes that occur in association with the development of cancer (identified in aim 1) may play a role promoting carcinoma initiation and tumor growth, and therefore may represent novel targets for cancer prevention and screening strategies. Aim 2 will provide an understanding of immune

microenvironment changes that occur during carcinoma development specifically in never smokers, as these may differ from those in patients who have previously smoked. Aim 3 will provide insight into how tumor immune microenvironments differ between never and former smoking lung cancer patients. Aims 2 and 3 both contribute to the discovery of unique features that may potentially be involved in tumor initiation or impact differential response to immunotherapy in never smoking patients.

This study will use bronchoalveolar lavage FFPE cell blocks from the pathology archives of Vancouver General Hospital. Specimens for this study will include those from 12 patients with lung adenocarcinoma and 12 patients with no cancer in their lungs. Each of these groups will include specimens from 7 never smoking patients and 5 former smoking patients (Tables 1 and 2). Ethics approval has been obtained (H24-00628) and slides have been reviewed for specimen adequacy. All included patients had pulmonary nodules/masses on imaging with a potentially malignant initial appearance. All specimens were culture-negative for infectious organisms, such that the imaging findings could not be attributed to an active infectious process instead of malignancy. The patients with lung cancer had diagnosis confirmed on tissue sampling, but had a bronchoalveolar lavage specimen without malignant cells. Testing only these 'false negative' specimens ensures profiling is of the non-neoplastic cells and therefore that results are applicable to patients who cannot be diagnosed via standard cytologic assessment of these samples. The patients without cancer had at least two years of follow-up confirming benign status, and the patients with cancer were identified from the same timeframe, preventing specimen age from confounding results. All specimens were collected within the last 4 years, well within the assay's recommended 10 year maximum specimen age. Smoking history including pack-year exposure was available from medical records. Patients with current smoking, autoimmune disease, immunodeficiency or transplanted organs were excluded to minimize potential confounders in this small pilot study; representatives of these groups will be included in subsequent validation studies.

Per the timeline in Table 3, RNA will be extracted from each sample and **assessed using a NanoString PanCancer Immune Profiling nCounter Assay (782 genes)** through collaboration with MAPcore (a UBC core facility) and the VGH clinical molecular laboratory, using in-house protocols already optimized for FFPE samples. We hypothesize that signatures related to M2 macrophage polarization, humoral immunity, protease activity and bone marrow-derived macrophages (rather than tissue-resident macrophages) will be associated with malignancy, and these signatures are covered by the proposed NanoString panel. This panel also includes IL-1β, hypothesized to be a key mediator of lung cancer development in never smokers.

Test extractions show large RNA yields from bronchoalveolar lavage specimens with similar cellularity and specimen age as those to be used for this study (yields of 650 to 1500 ng per sample, with only 25-300 ng needed per NanoString assay). Samples from patients with vs. without cancer will be compared to identify a signature predictive of malignancy. Results of never vs. former smoker analysis will be interpreted regarding pro- and anti-tumorigenic pathway activity, for identification of pro-tumorigenic pathways that could be pharmacologically inhibited, and for assessment of pathways impacting immunotherapy response.

The signature predictive of malignancy will be validated using a small custom NanoString panel covering selected genes of greatest predictive value, applied to 12 additional bronchoalveolar lavage samples identified from the pathology archives. This custom panel assay could then form the basis of a clinical test applied to bronchoalveolar lavage specimens for prospective validation in future studies.

Impact statement:

The expected outcomes of this study are that we will have (i) developed a clinically translatable gene expression signature predictive of malignancy and (ii) characterized how tumor associated immune microenvironments differ in never vs. former smoking patients. As bronchoalveolar lavage is a common part of routine care, testing on these specimens can impact a large population without requiring additional procedures or patient participation beyond the standard of care. FFPE cell blocks are already routinely prepared for microscopic examination of cell morphology, with no retention of unfixed cells. Suitability of our test to FFPE material enables specimens to first be assessed through uncompromised standard of care cytomorphologic assessment, with subsequent triage to additional testing if necessary. A NanoString assay such as we propose could be incorporated with other NanoString assays currently performed weekly in our clinically accredited hospital laboratory. This opportunity for rapid translation to a clinically feasible test has the potential for sustained and powerful impacts on patient care, by providing more accurate and timely prediction of whether a pulmonary nodule is malignant. Such predictions may reduce unnecessary surgery for benign nodules and expedite biopsy or surgery for nodules with a high probability of malignancy.

Our characterization of immune cell activity in never vs former smokers will contribute to our understanding of the pathogenesis of lung cancer in never smokers, foundational for the development of risk reduction strategies and preventative therapies in this population. Never smoking patients are currently not eligible for screening programs and are in need of novel early diagnosis and prevention strategies. We hypothesize that IL-1β activity, which has been associated with air pollution exposure[7], may be elevated in never-smoking patients with lung cancer. Confirmation of this hypothesis would contribute to literature supporting IL-1β inhibition as a possible avenue of lung cancer prevention.[16] Our analysis will also inform on factors that may contribute to differential immunotherapy response in never vs former smokers for refinement of treatment approaches.

Overall we propose a clinically relevant and readily translatable project working to accelerate our understanding of lung cancer pathogenesis and achieve earlier and safer lung cancer diagnosis for never and former smoking patients.

Public Summary:

Nodules may be detected on imaging of the lungs performed for lung cancer screening or for investigation of patient symptoms. Cancerous and non-cancerous nodules (such as scars from prior infection) can be indistinguishable on imaging. Safely and promptly determining whether a lung nodule is likely to be cancerous or not is critical for enabling high risk nodules to proceed to cancer characterization (e.g through tissue biopsy) and appropriate treatment, and for avoiding unnecessary procedures and anxiety in patients with very low risk nodules. The need for earlier detection and efficient diagnostic pathways is heightened among never smoking patients, as they are not eligible for screening programs.

Lung cancers grow in association with immune system cells that can promote tumor initiation and growth. However, it remains poorly understood which immune cells are involved in lung cancer development and whether the immune cells involved are different in people who have never smoked compared to people who have smoked. We predict that the immune cells near a tumor are different than those in lungs with non-cancerous nodules, and that characterization of these immune cells can contribute to our understanding of cancer development.

We propose to (i) develop a test that can be performed on immune system cells collected from lung airspaces for prediction of whether the lung has cancer, potentially enabling earlier and safer lung cancer diagnosis and (ii) characterize differences in immune cells between never and former smoking patients. Our study will provide a better understanding of the changes in immune cell composition that may contribute to cancer development, and will provide an understanding of how these processes differ depending on whether the individual has previously smoked. Determining these differences may suggest new avenues for early cancer detection and cancer prevention in the never smoking population. As current treatments of lung cancer often involve agents that affect recognition of the cancer cells by the immune system, understanding differences in immune system cells associated with cancer in never vs. former smokers is also relevant to understanding potential differences in treatment response between these groups.

To achieve these aims, we will assess 782 genes with immune system related functions using a technique routinely performed in our clinical molecular laboratory (NanoString assays). Previously collected clinical specimens with residual material will be used as input. The specimens to be used were collected from bronchoalveolar lavage, a common procedure in which lung airspace cells are collected through the airways under sedation. We will assess differences in gene expression in samples from patients with vs. without lung cancer, and from patients with vs. without prior smoking. A custom assay containing just the genes most predictive of cancer will then be used to assess reproducibility of our findings in a separate set of samples. Never and former smoking patient samples will also be analyzed for possible tumor promoting signatures, with attention to signals relevant to therapy response, tumor initiation and cancer prevention.

Budget:

Discovery Set (necessary to identify genes of most interest for malignancy prediction and smoking status correlates, using a large panel of immune-related genes):

- Retrieval of blocks from clinical archives: $12.50 x 24 samples = $300
- RNA extraction (including reagents and technician time): $60 x 24 samples = $1,440
- NanoString nCounter PanCancer Immune Response Panel: $4729 for 12 reactions x 2 kits = $9,458
- NanoString master kit: $450 for 12 reactions x 2 kits = $900
- NanoString shipping and handling: $407
- Technician time for NanoString assays: $1,536

Total for discovery set: $13,791

Validation Set (for validation of the predictive value of the small panel of genes of interest, critical for clinical translation of findings):

- Retrieval of blocks from clinical archives: $12.50 x 12 samples = $150
- RNA extraction (including reagents and technician time): $60 x 12 samples = $720
- Custom probe set ($244/gene x 35 genes x minimum order of 96 reactions) =$8,540
- NanoString master kit: $450 for 12 reactions
- NanoString shipping and handling: $204
- Technician time for NanoString assays: $895

Total for validation set: $10,709

Total budget: $25,000

The requested funds are critical to cover the costs of discovery-set assays and the validation custom probe set. The Principal Investigator is an early career MD/PhD clinician scientist working to establish an independent research program based on this pilot study. Data from this project will be a central element of future funding applications for further validation and clinical translation of findings.

This project is also supported by $3000 of funding from the Diagnostic and Molecular Pathology residency training program, which will be used to support knowledge translation (eg open access publication fees and conference registration).

Personnel: This project will be completed by the co-investigators listed, along with the expert technical staff at the Vancouver General Hospital Clinical Molecular Laboratory and Molecular and Advanced Pathology Core (MAPcore, technician time budgeted for above). The Principal Investigator Dr. Naso is an actively practicing MD/PhD thoracic pathologist with 30% protected time for research that can be dedicated to this project. Dr. Naso is experienced in NanoString assay data analysis from prior projects (manuscripts in preparation). The co-investigators represent expertise in thoracic surgery (Dr McGuire, MD, MSc), diagnostic and molecular pathology (Dr Trinder, MD/PhD), bioinformatics (Dr Lim, PhD) and experimental biology (Dr Lockwood, PhD), and are committed to supporting this project. Data analysis will be led by pathology resident and MD/PhD graduate Dr. Trinder, who has support from the residency program for dedicated research time to complete this project. Dr Lim, a professor and

bioinformatician who focuses on how environmental exposures associate with lung cancer, will support the bioinformatic analysis. Correlations with never smoking lung cancer pathobiology will also be assisted by Peiyao Wang, a PhD student supervised by co-investigator Dr Lockwood, whose thesis focuses on characterizing molecular features of lung cancer in never smokers. This project is central to the research interests and expertise of our team. The interdisciplinary nature of our team enables us to pair robust science with practical clinical translation.

APPENDIX

Table 1: Final diagnosis of patients whose bronchoalveolar lavage specimens will be in the discovery set.

ID	Cohort	Smoking History	Final Diagnosis of Lung Nodule
1	Malignant	Never	Adenocarcinoma, lepidic
2	Malignant	Never	Adenocarcinoma, acinar
3	Malignant	Never	Adenocarcinoma, lepidic
4	Malignant	Never	Adenocarcinoma, not otherwise specified
5	Malignant	Never	Adenocarcinoma, mucinous
6	Malignant	Never	Adenocarcinoma, micropapillary
7	Malignant	Never	Adenocarcinoma, mucinous
8	Malignant	Former	Adenocarcinoma, mucinous
9	Malignant	Former	Adenocarcinoma, solid
10	Malignant	Former	Adenocarcinoma, not otherwise specified
11	Malignant	Former	Adenocarcinoma, not otherwise specified
12	Malignant	Former	Adenocarcinoma, not otherwise specified
13	Benign	Never	Sarcoidosis
14	Benign	Never	Scar/atelectasis
15	Benign	Never	Probable sarcoidosis
16	Benign	Never	Probable sarcoidosis
17	Benign	Never	Sarcoidosis
18	Benign	Never	Probable organizing pneumonia
19	Benign	Never	Probable organizing pneumonia
20	Benign	Former	Resolved on follow-up imaging
21	Benign	Former	Resolved on follow-up imaging
22	Benign	Former	Fibrotic nodule, aspiration vs interstitial lung disease associated
23	Benign	Former	Nodular scar
24	Benign	Former	Stable nodule, likely post-infectious or inflammatory

Table 2: Clinical and pathologic features of patients whose bronchoalveolar lavage specimens will be in the discovery set.

Specimen category	Age [median, range]	Female [n, %]	Nodule size (cm) [median, range]	Clinical stage [n, %]			
				I	II	III	IV
Malignant							
Never smoking	80 (58-88)	5 (71)	2.9 (1.8-3.7)	5 (71)	1 (14)	0 (0)	1 (14)
Former smoking	68 (61-81)	2 (29)	3.6 (0.9-9.5)	2 (29)	0 (0)	2 (29)	1 (14)
All malignant cases	76.5 (58-88)	7 (58)	2.9 (0.9-9.5)	7 (58)	1 (8)	2 (17)	2 (17)
Benign							
Never smoking	58 (35-74)	5 (71)	1.9 (0.8-3.8)	NA	NA	NA	NA
Former smoking	72 (65-85)	2 (29)	2.5 (1.3-4.4)	NA	NA	NA	NA
All benign cases	67 (35-85)	7 (58)	2.1 (0.8-4.4)	NA	NA	NA	NA

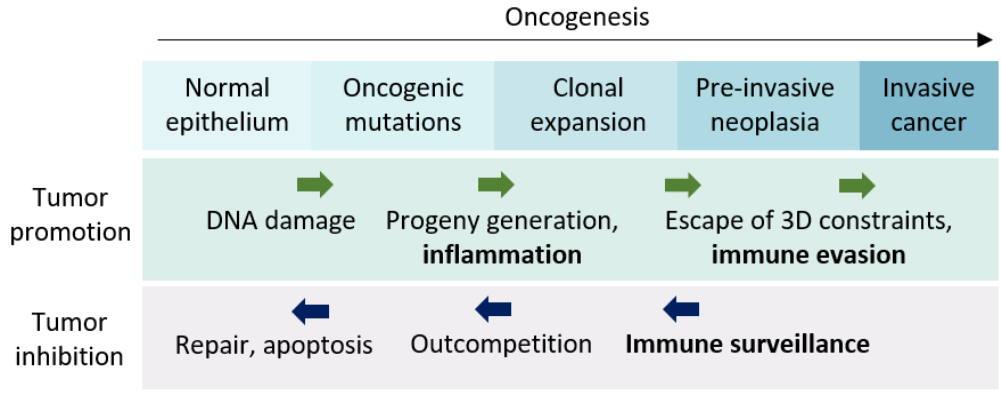
NA = not applicable.

Table 3: Timeline for the proposed study

Deliverable	2024		2025			
	Nov/ Dec	Jan/ Feb	Mar/ Apr	May/ June	Jul/ Aug	Sept/ Oct
Acquisition of reagents & retrieval of cell blocks						
RNA extraction and NanoString assay runs						
Gene expression data analysis & custom assay design						
Validation set RNA extraction and custom assay runs						
Preparation for knowledge dissemination						

Knowledge dissemination activities will include presentation at the Canadian Lung Cancer Conference in early 2026, or another Canadian conference

Figure 1: Interactions with immune cells play key roles in promoting and constraining oncogenesis. We hypothesize that differences in immune cell activity will be present in lungs with carcinoma compared to those without. This figure is adapted from a publication of co-investigator Dr. Emilia Lim.[17]



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September 3, 2024

Re: Geoffrey Ogram Memorial Research Grant Application of Dr Julia Naso

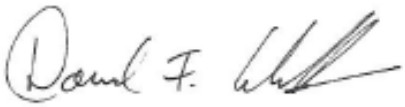
Dear Lung Cancer Canada Team:

This letter is in support of the application of Dr. Julia Naso, a consultant Anatomical Pathologist at VGH and UBC Clinical Assistant Professor. I confirm that her proposed project is feasible within our institution and its collaborating research centers.

We are closely affiliated with the Molecular and Advanced Pathology Core (MAPcore), a clinically accredited core facility which collaborates with the clinical molecular laboratory to run NanoString assays. Dr. Naso herself has 30% protected time for research. As a teaching center for residents and medical students, our department also supports and encourages trainee involvement in research projects such as this.

I am confident that our institution and affiliated centers can provide the resources needed to support Dr. Naso's proposed project.

Sincerely,



David F. Schaeffer, MD FRCPC
Head, Department of Pathology and Laboratory Medicine | Vancouver General Hospital
Pancreatic Cancer Research Chair at Vancouver General Hospital
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THE UNIVERSITY OF BRITISH COLUMBIA

RESEARCH PROJECT INFORMATION FORM

For Administration Use Only		
FAS #: F24-04627	Grant #:	Date Received: Sep 16, 2024

This form has been designed to be completed using Adobe Acrobat or Adobe Reader.
1) For *government and non-profit grant applications* and *UBC internal funding applications*, please submit this form to the **Office of Research Services**, #102-6190 Agronomy Road, Vancouver, BC V6T 1Z3 or ors@ors.ubc.ca. **Applications must be submitted to ORS at least two full working days prior to the sponsor competition deadline to ensure that they can be reviewed**. See www.ors.ubc.ca/internal-deadlines.
2) For *all other funding*, please submit to the **University-Industry Liaison Office**, #103-6190 Agronomy Road, Vancouver, BC V6T 1Z3 or urg@uilo.ubc.ca.
3) ***For the UBC Okanagan Campus***, please submit to 336 Fipke Building, 3333 University Way, Kelowna, BC Canada V1V 1V7.

A. UBC Principal Investigator

Name: Julia Naso | Faculty: Medicine
Tel: 604-875-4111 ext 68252 | Department: Pathology and Laboratory Medicine
Email: julia.naso@vch.ca | Division: Anatomical Pathology
Academic Rank: Clinical Assistant Professor | Is this a term position? ○ Yes ◉ No

B. Project Details

Attach a full copy of the application form, or a budget and proposal/workplan if an application form is not required.

Title: Expediting Lung Cancer Diagnosis and Understanding Immune Dysregulation in Never and Former Smoking Patients

Original Funding Source: *(Where project's funds originate)* Geoffrey Ogram Memorial Research Grant (Lung Cancer Canada)

Primary Funding Source: *(from where UBC is receiving project funds)*
◉ Same as Original Funding Source above
○ Other. Please specify:

All additional funding sources: *(if applicable)*

Funding Program (if applicable):
Application Deadline (if applicable): Sept 30, 2024
If this is a student or trainee fellowship, please enter recipient name:

Budget. Please detail **all cash** to be received by UBC for this project **(do not include in-kind contributions)**
The PI must include indirect costs as per UBC Policy LR2. Visit **www.research.ubc.ca/indirect-costs** for more details.

	Direct Costs:$	Indirect Costs:$	Total Cash:$
☐ Government			
☒ Non-profit	25,000		25,000
☐ Industry			
☐ UBC (Internally-funded)			

If an administrative unit fee has been included as a direct cost, please specify the rate: 0% per sponsor (SZ)

Project length (months): 12

If this project is primarily conducted at an approved institute or centre, please select: Vancouver Coastal Health Research Institute
In which faculty/department/division/institute or centre will the Grant be set up?: Pathology and Laboratory Medicine

Indicate main Institutions (UBC or formally affiliated institution) where research activity for the project will be undertaken (% at each):

☐ UBC Vancouver Campus % ☐ UBC Okanagan Campus % ☐ Interior Health Authority %
☐ BC Cancer Agency % ☐ BC Centre for Disease Control % ☐ Providence Health Care Research Institute %
☐ BC Mental Health & Substance Use Services Research Institute % ☐ Women's Health Research Institute %
☐ BC Children's Hospital Research Institute % ☐ Fraser Health Authority % ☒ Vancouver Coastal Health Research Institute %

For non-clinical projects, all funding will be held at UBC. *If this is a clinical project*, please indicate where the Grant will be held:
☑ UBC ☑ Other (please specify):

C. Resource Implications

Building(s) and Room(s) to be used as research space for this project: Clinical office of Dr Naso at Vancouver General Hospital - per email(SZ)
Resource implications for: ☐ Dept or School ☐ Centre ☐ Dept/School & Centre (required for Life Sciences Centre) ☐ To be confirmed

Mandatory only for Faculty of Medicine
Is this a community-based research project? ◉ No ○ Yes
Will HQP be involved in the Project? ○ No ◉ Yes ○ Don't know If yes, please indicate estimated numbers below.
Undergraduate Students:____ Graduate Students:____ Post-docs:1 Technicians:____ Research Associates:____ Other:____

D. Certifications & Approvals

Does the project involve the use of humans, animals or biohazardous materials?

◯ No - Please proceed to **Section E** ◉ Yes The project requires a Certificate of Approval referencing the exact project title, collaborator and sponsor names. Please provide certificate/approval details or indicate "pending" below:

The Project involves the following (please select all that apply):

	Certificate/Application Number		Certificate/Application Number
☑ Humans	H24-00628	☐ Animals	
☐ Clinical Study Drug		☐ Biohazardous Materials	
☐ Clinical Study Device		☐ Radioactive Materials	
☐ Hospital Review		☐ Environmental Impact	

Please login to RISe rise.ubc.ca to submit an amendment to add this Project to an existing approval.

E. Type of Funding

Is this Research Project Information Form accompanying an attached **grant application form**?

◯ No - Please proceed to **Section F** ◉ Yes - Please go to **Section I** (Signatures)

F. Contact (for Primary Funding Source identified in Section Bii)

Company/Organization:	Contact Name:
Tel: Fax:	Address:
Email:	

G. Conflict of Interest

Are you aware of any conflicts of interest that may have a bearing on this project?

◯ No - please proceed to **Section H** ◯ Yes - please check applicable boxes below:

	UBC Principal Investigator	UBC Co-Investigator(s)	UBC Student(s)
Seat on Board of Directors	☐	☐	☐
Seat on Scientific Advisory Board	☐	☐	☐
Any Role within the Company	☐	☐	☐
Shares in Sponsor Company	☐	☐	☐
License / Option Agreement	☐	☐	☐
Non-Disclosure Agreement	☐	☐	☐
Consulting Agreement	☐	☐	☐

☐ Other conflicts of interest:

Please note that all conflicts of interest and conflicts of commitment must be disclosed annually and managed as per UBC Policy SC3.

H. Additional Information

Will you be using any proprietary or confidential materials or information in the project?

◯ No ◯ Yes - please specify:

Source of Material:

Nature of Material:

Are you conducting any research for another collaborator or sponsor that might overlap with this project?

◯ No ◯ Yes - please describe below:

Will any employees of the collaborator or sponsor be participating in the project? ◯ No ◯ Yes

If yes, will they be participating on site at UBC? ◯ No ◯ Yes

I. Signatures

In accordance with UBC LR2, holders of UBC research Grants must be members of the permanent academic staff. For details on exceptions, please refer to LR2 #4.1.1 to 4.14.

Principal Investigator

I understand that Indirect Costs must be included in the budget as per UBC Policy LR2.

Signature: [signature]

Or click box to add scanned signature

Name: Julia Naso

Date: 9/15/24

I hereby authorize a Grant to be set up for each funding source listed in Section B. as required, with indirect costs recovered as specified in the budget section of this document.

Department / Unit Head or authorized signatory	**Centre Director** required for all research projects primarily involving a Centre or Institute	**Dean** (not required in the UBC Vancouver Faculties of Science or Applied Science) or authorized signatory
Signature: zu-hua gao	Signature:	Signature:
Or click box to add scanned signature	Or click box to add scanned signature	Or click box to add scanned signature [signature]
Name: Dr. Zu-hua Gao	Name:	Name: Dr. Teresa S.M. Tsang
Title: Department head	Date:	Title: Associate Dean Research Faculty of Medicine University of British Columbia
Date: 9/15/2024	Centre or Institute:	Date: September 18th, 2024
For industry and non grant funding only	**For industry and non grant funding only**	**For industry and non grant funding only**
I also authorize future budget increases as may be applicable for this project Initials:	I also authorize future budget increases as may be applicable for this project Initials:	I also authorize future budget increases as may be applicable for this project Initials:
Or click box to add scanned signature	Or click box to add scanned signature	Or click box to add scanned signature
I cap the budget increase amount without further signatures at: $	I cap the budget increase amount without further signatures at: $	I cap the budget increase amount without further signatures at: $

For Faculty/Department Use – for internally funded projects, attach project summary and budget pages and provide the following information:

Funding Source Account Worktag: Is source Account Worktag restricted? ◯ Yes ◯ No

Project Start Date: Project End Date:

For internally-funded projects, should remaining funds at end of project be returned to the funding source Account Worktag? ◯ Yes ◯ No

Signature of signing authority for funding source Account Worktag:

Or click box to add scanned signature

Name:

Date:

For Research Services (ORS) Internal Use Only

Director (ORS) Signature: [signature]

Name: Susan O'Neil Manager, Research for Sharon Wu
Managing Director, Research Support Services
Office of Research Services
The University of British Columbia

Date: September 20, 2024