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January 20th, 2025

Dear adjudication committee for the *Lung Ambition Awards*,

The Microfluidics and Nanotechnology (MiNa) laboratory at the University of Victoria is seeking $50,000 in funding to support the development of a new saliva-based biosensor for simple, non-invasive, and accessible lung cancer screening.

Although Canada's efforts to offer lung cancer screening has significantly reduced cancer mortality rates, over 70% of lung cancers are still diagnosed when they are already at stage III or IV. As the 5-year survival rate for lung cancer decreases drastically between ascending stages, detecting cancer in the earlier stages generally offers a better prognosis. Currently, lung cancer screening is restricted to those within their mid-fifties to mid-seventies with a significant history of smoking. Additionally, this screening is only provided once every one or two years. Not only does this provide time for the cancer to grow, but also misses the 10-20% of lung cancers that develop in non-smoking individuals.

Our priority is to develop simple, non-invasive screening technology that can encourage the frequent testing of individuals of all backgrounds. The goal of this preliminary screening is to support the detection of lung cancer while it's in its early stages, allowing for medical intervention to occur much earlier in cancer development. The proposed technology is a specially designed electrochemical sensor that is adapted to selectively respond to lung cancer biomarkers found in saliva. Unlike most biosensors which optimize analyte detection based on a single biomarker, this sensor will simultaneously respond to multiple biomarkers, allowing for improved accuracy and sensitivity.

The MiNa lab specializes in the development of advanced sensing methods to detect analytes found in complex environments. Previously, we have focused on the development of biosensors for the *Cryptosporidium* pathogen, microfluidic-enhanced gas detection systems for analytes such as cannabinoids, nuisance gases, and natural gas compounds, and microfluidic-based platforms for the identification and quantification of microplastics within water samples. The primary doctorate student working on this project has a history of contributions to the biosensor field, focusing on applications in glucose monitoring and early prostate cancer detection.

We are seeking $50,000 in funding to directly contribute to the development of an innovative lung cancer screening tool, advancing non-invasive diagnostics and improving early detection rates. The funds will be used to support our doctorate student, acquire research materials, and allow for sensor characterization through techniques such as scanning electron microscopy and Raman spectroscopy.

Thank you for the opportunity to submit this proposal. Should you have any questions or would like additional information, please don't hesitate to contact me using the details below.

Yours truly,

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Introduction

Background: For diseases such as lung cancer, an early diagnosis can greatly impact the likelihood of a successful treatment. Although there are measures in place to support early diagnosis, such as through low-dose CT-based cancer screening, screenings are often only performed within specific average-risk age clusters. In order to be a candidate for lung cancer screening in Canada, you must be between the ages of 55 and 74 and have a significant history of smoking. Not only is this screening only available in certain provinces, but it also misses the estimated 10 - 20% of lung cancer cases each year that occur in non-smoking individuals [1]. Even with CT-based cancer screening, approximately 70% of lung cancers are still diagnosed when they are already at stage III or stage IV; at this point, cancer has usually spread beyond the lung and the 5-year survival rate drops to 16% and 3%, respectively [2].

Significance: If lung cancer could be detected with less-invasive and less-resource intensive means, not only would this allow for an increased frequency of testing, but this would also permit lung cancer screening to cover a wider range of individuals; potentially detecting lung cancer earlier on in its development. We aim to support this reality through the development of biosensors capable of identifying lung cancer through biomarkers present in saliva.

Proposed Methodology

Biomarker Selection: Recently, microRNAs (miRNAs) - small RNA fragments associated with gene expression, have been found to be a potentially useful class of biomarker for cancer detection [3]. During cancer development and progress, certain miRNAs become dysregulated due to their role in either tumour suppression or growth [4]. These dysregulated miRNAs are occasionally secreted into the extracellular space and become circulating miRNA, finding their way into various bodily fluids such as plasma, breast milk, tears, and saliva [5, 6].

Many research groups are further analyzing the relationship between different miRNAs and lung cancer specifically. Although there are upwards of 16 different miRNAs being explored for their connection to lung cancer, miRNA-141 and miRNA-21 have proven to be particularly intriguing [7]. In one study, analysis on miRNA-141 levels in plasma was found to have a 98% specificity in recognizing early non-small cell lung cancer (NSCLC) patients against controls and miRNA-21 was found to be positively correlated with cancer stage [8]. This suggests that these two biomarkers could be used in tandem to not only identify NSCLC early on, but also effectively monitor its progression or regression over time. Additionally, miRNA-21 and miRNA-141 have proven ability to be identified within and extracted from saliva, making them excellent candidates for saliva-based screening [9, 10].

Sensing Technology: Electrochemical-based sensing has become a staple sensing methodology for miRNA bio-detection due to its affordability, adaptability, and ease of enhancement and use [11]. While it primarily holds popularity for detection within serum or plasma, researchers have found that saliva-based detection may be equally as favourable due to comparable miRNA concentrations [12]. By bolstering the sensitivity and selectivity of the sensor through sensing layer modifications, we aim to develop a sensor that is specifically able to respond to miRNA-21 and miRNA-141 at concentrations present in saliva. The proposed modifications include the addition of two layers onto the sensing surface: layer 1 consisting of doped monolayer graphene oxide to boost both the current density and the sensing surface area, followed by layer 2, which will be comprised of a novel metal-polymer hybrid imbued with capture probes specific to the selected miRNAs (Fig. 1). The goal of the secondary layer is to combine the advantageous conductivity properties of nanoscale noble metals and the high flexibility, large surface area, and biomolecule immobilization ability of polymers.

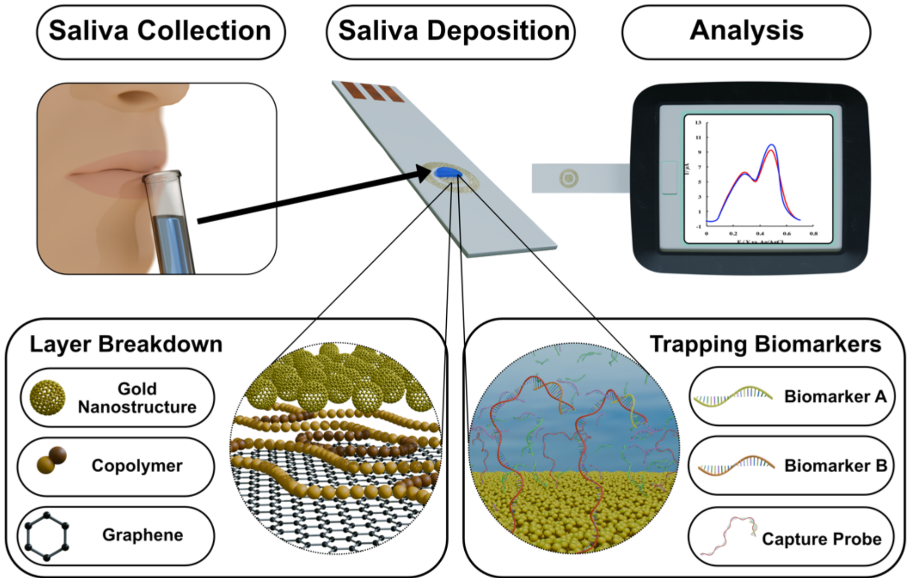

Figure 1. Electrochemical Sensor Breakdown and Use

The electrochemical sensor will be tested with a variety of electrochemical techniques such as cyclic voltammetry, linear sweep voltammetry, differential pulse voltammetry, electrochemical impedance spectroscopy, and chronoamperometry to determine the sensing methodology that provides the highest accuracy in synthetic saliva samples. It will also be analyzed using characterization techniques such as scanning electron microscopy, Fourier-transform infrared spectroscopy, and x-ray diffraction, amongst others.

Conclusion

Expected Results: The result of this work will be a multi-capture hybrid electrochemical sensor that will be able to identify and quantify various concentrations of miRNA-21 and miRNA-141 in saliva. The ultimate goal of this work is to create a sensor with the ability to both detect and track lung cancer progress in a method that is inexpensive, simple to use, and accurate, with the aim of increasing lung cancer screening availability within Canada.

References

[1] R. A. Murphy et al., “Lifestyle factors and lung cancer risk among never smokers in the Canadian Partnership for Tomorrow’s Health (CanPath),” Cancer Causes Control, vol. 33, no. 6, pp. 913–918, Jun. 2022, doi: 10.1007/s10552-022-01566-x. **[2]** S. C. Government of Canada, “Five-year cancer survival by stage at diagnosis in Canada.” Accessed: Feb. 04, 2025. [Online]. Available: https://www150.statcan.gc.ca/n1/pub/82-003-x/2023001/article/00001-eng.htm **[3]** G. A. D. Metcalf, “MicroRNAs: circulating biomarkers for the early detection of imperceptible cancers via biosensor and machine-learning advances,” Oncogene, vol. 43, no. 28, pp. 2135–2142, Jul. 2024, doi: 10.1038/s41388-024-03076-3. **[4]** B. M. Hussen, H. J. Hidayat, A. Salihi, D. K. Sabir, M. Taheri, and S. Ghafouri-Fard, “MicroRNA: A signature for cancer progression,” Biomedicine & Pharmacotherapy, vol. 138, p. 111528, Jun. 2021, doi: 10.1016/j.biopha.2021.111528. **[5]** H. Wang, R. Peng, J. Wang, Z. Qin, and L. Xue, “Circulating microRNAs as potential cancer biomarkers: the advantage and disadvantage,” Clinical Epigenetics, vol. 10, no. 1, p. 59, Apr. 2018, doi: 10.1186/s13148-018-0492-1. **[6]** J. O’Brien, H. Hayder, Y. Zayed, and C. Peng, “Overview of MicroRNA Biogenesis, Mechanisms of Actions, and Circulation,” Front Endocrinol (Lausanne), vol. 9, p. 402, Aug. 2018, doi: 10.3389/fendo.2018.00402. **[7]** D. Canatan et al., “MicroRNAs as a biomarker in lung cancer,” Acta Biomed, vol. 94, no. 1, p. e2023045, 2023, doi: 10.23750/abm.v94i1.13334. **[8]** A. Arab et al., “Potential circulating miRNA signature for early detection of NSCLC,” Cancer Genetics, vol. 216–217, pp. 150–158, Oct. 2017, doi: 10.1016/j.cancergen.2017.07.006. **[9]** Garg, A., Urs, A.B., Koner, B.C. et al. “Evaluation of Diagnostic Significance of Salivary miRNA-184 and miRNA-21 in Oral Squamous Cell Carcinoma and Oral Potentially Malignant Disorders”. Head and Neck Pathol 17, 961–968 (2023). https://doi.org/10.1007/s12105-023-01600-7 **[10]** V. Grassia et al., “Salivary microRNAs as new molecular markers in cleft lip and palate: a new frontier in molecular medicine,” Oncotarget, vol. 9, no. 27, pp. 18929–18938, Apr. 2018, doi: 10.18632/oncotarget.24838. **[11]** M. El Aamri, G. Yammouri, H. Mohammadi, A. Amine, and H. Korri-Youssoufi, “Electrochemical Biosensors for Detection of MicroRNA as a Cancer Biomarker: Pros and Cons,” Biosensors (Basel), vol. 10, no. 11, p. 186, Nov. 2020, doi: 10.3390/bios10110186. **[12]** L. Hofmann et al., “Comparison of plasma- and saliva-derived exosomal miRNA profiles reveals diagnostic potential in head and neck cancer,” Front Cell Dev Biol, vol. 10, p. 971596, Aug. 2022, doi: 10.3389/fcell.2022.971596.

Impact Statement

The development of a saliva-based biosensor for lung cancer detection will offer simple, non-invasive, and accessible lung cancer screening - allowing for a wider screening pool and more frequent testing. This will permit the detection of lung cancer cases that would have been missed within traditional screening limitations and will support the possibility for earlier medical intervention, providing the greatest opportunity for improved patient outcome.

Public Summary

The need for improved medical technologies, treatments, and diagnostic systems remains an engineering challenge as society continues to expand. Recently, a shift has been made for the push for medical technologies to be non-invasive or as minimally invasive as possible. Not only does this increase patient compliance, but can allow for simpler testing procedures, decreasing the need for certified technicians and increasing the frequency of testing.

For diseases such as lung cancer, an early diagnosis can greatly impact the likelihood of a successful treatment. Although there are measures in place to support early diagnosis, such as through low-dose CT-based cancer screening, screenings are often only performed within specific average-risk age clusters. In order to be a candidate for lung cancer screening in Canada, you must be between the ages of 55 and 74 and have a significant history of smoking. Not only is this screening only available in certain provinces, but it also misses the estimated 10 - 20% of lung cancer cases each year that occur in non-smoking individuals. Even with CT-based cancer screening, approximately 70% of lung cancers are still diagnosed when they are already at stage III or stage IV; at this point, cancer has usually spread beyond the lung and the 5-year survival rate drops to 16% and 3%, respectively.

Saliva, like other bodily fluids, holds a vast amount of information about human health and can be used to test for various viral infections and drug or alcohol usage. Although saliva isn't currently being used to assess as many conditions as blood is, researchers have found that certain disease markers that exist in blood are also present in saliva. Notably, some of the markers that can be found in both blood and saliva have a correlation to lung cancer, suggesting that if a detection system could be made accurate enough, there may be a way to identify and monitor lung cancer status through blood or saliva sampling.

We aim to make this a reality through the development of an extremely sensitive sensor designed to selectively respond to these lung cancer markers found in saliva, allowing the potential for less-invasive and less-resource intensive lung cancer screening options. This technology has the potential to revolutionize lung cancer detection by encouraging cancer screening for individuals of all ages and smoking histories, catching cancer cases that may have been missed within current screening limitations. It will also support an increased testing frequency, enabling earlier medical intervention and improving patient survival rates. Overall, the development of this sensor aspires to assist in the simple, efficient, and non-invasive screening for lung cancer, encouraging rapid detection and treatment to support the best patient outcome.

Budget Justification
The total proposed budget for this project is $50,000, 80% of which is dedicated to student support, 8% to necessary research materials, 10% to cover various characterization equipment usage fees, and 2% to anticipated travel costs related to conference attendance.

1. **Student Support**
   A budget of $40,000 is allocated towards financial expenses for one doctoral (PhD) student (Abbas Sabahi) which is based on the current Tri-Agency Scholarship amount for graduate students. The PhD student has a strong background in biosensor development, having worked on electrochemical-based sensors for both glucose monitoring in blood and the detection of prostate cancer using serum samples. The student's work on prostate cancer detection also focused on microRNA-based detection, proving his capabilities to develop and optimize sensors for microRNA specific capture and response. The development of this sensor is the focus of the student's thesis, indicating their fulltime commitment to the project.

2. **Materials**
   A total budget of $4,000 is allocated towards material costs which will go towards the purchasing of electrodes, chemicals required for the modification of the sensing layer (e.g., doped graphene, compatible forms of gold, capture probes), and chemicals required to assess the sensor, such as those used to make artificial saliva solution. It will also go towards the purchase of specialized labware, such as a laboratory condenser, that will be required for various chemical processes.

3. **Equipment Usage**
   A total budget of $5,000 is allocated towards user fees for various material characterization equipment, including scanning electron microscopes, Raman spectroscopy systems, Fourier-transform infrared spectroscopy systems, and x-ray diffraction machines. At the University of Victoria, the user fees for these machines are on average $70/hour but may increase upon the need for specific training or required surface treatments before use. We are allotting roughly 60 hours of equipment usage, including leeway for special cases where additional training or treatments are required.

4. **Travel Support**
   A total budget of $1,000 is allocated towards covering travel related expenses for the PhD student to participate in a relevant Canadian conference.

Investigators
- **Primary Investigator:** Mina Hoorfar
  - **Student Investigator:** Abbas Sabahi

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February 7, 2025

Lung Cancer Canada
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Dear Lung Ambition Awards review committee,

On behalf of the University of Victoria, I am pleased to provide this letter of support for Mina Hoorfar's application entitled "An Electrochemical Biosensor for Detection of Lung Cancer Biomarkers in Saliva". Upon successful completion of the project, the team will have completed preliminary research and development on an electrochemical-based biosensor for lung cancer detection through saliva samples, opening pathways regarding the possibility of simple, non-invasive lung cancer screening.

I confirm that the proposed research is feasible to conduct here at the University of Victoria.

In the *Microfluidics and Nanotechnology Lab*, the *Brolo Lab*, and the *Centre for Advanced Materials and Related Technology* at the University of Victoria, the investigators have access to resources and equipment that are necessary to carry out this project, such as a scanning electron microscope, a Raman spectroscopy system, an x-ray diffractometer, a Fourier-transform infrared spectroscopy system, and a potentiostat.

We look forward to a successful outcome.

Sincerely,

Fraser Hof, PhD
Associate Vice President Research
University of Victoria