DALHOUSIE UNIVERSITY

September 28, 2022

Dr. Alain Moreau, Director,
Network for Canadian Oral Health Research
Université de Montréal/ CHU Sainte-Justine Research Centre
3175 Chemin de la Côte-Ste-Catherine
Montréal, QC, H3T 1C5

RE: Final Report: Network for Canadian Oral Health Research: New Frontier Seed Grant NFSG2019-17

Dear Dr. Moreau,

I am writing to provide a final report for the grant awarded to the project entitled "*Exploring the diversity in the microbiome of high-risk oral epithelial dysplasia as a predictor of malignant progression*".

As you are aware, this project experienced significant delays due to challenges of the COVID-19 pandemic that could not be anticipated at time of contract execution, including shutdowns and global consumable shortages of laboratory supplies. Despite these challenges, the project successfully moved forward, owing to both the resiliency of our research team and your generous support. I would like to again offer my sincerest thank you to you and the NCOHR-RCRSB New Frontier Seed Grant Program review committee for granting a no-cost extension to this research, concluding June 30th, 2022. This extension allowed for completion of the project and for the funds to be spent as requested in the original application, including payment of sequencing services, salary support for the analyses, to allow submission of a manuscript and payment of open access publication fees.

Outcomes: Oral cancers pose a major public health challenge. There has been an increase in the number of studies that explore the association between cancer and the microbiome, and evidence that the microbiome may directly impact cancer progression is growing. Early detection is essential for improving the outcome of an oral cancer diagnosis and while an oral potentially malignant lesion is frequently a precursor to the development of oral cancer, well-characterized clinical samples with long follow-up data are required to establish relevant associations between the microbiota and disease. We used annotated archival swabs from 90 low-grade oral epithelial dysplasia (OED) samples – 30 from OED that progressed to cancer (cases) and 60 from OED that did not progress after a minimum of 5 years of follow up (matched control subjects) – along with other clinical data to show that archival lesion swabs can be used to analyse the microbiome using next-

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generation sequencing (16S rRNA gene amplicon sequencing). This is the first study to show that archival lesion swabs can be used to analyse the microbiome, and we also show that there are small but significant differences between those that progressed to cancer and those that did not.

Impacts on research capacity and training: This work supported the research capacity of an early career researcher (*Principal Investigator, L. Rock*) who brought together a new interdisciplinary research team of globally recognized experts and laboratories to create a foundational network that has generate new knowledge in the efforts to gain a better understanding of malignant transformation of oral dysplasia. Funding from this opportunity also provided project support and training support to a PhD student (*E. Marshall*) and an MSc student (*M. Pewarchuk*). The research experience that this work has provided has been of tremendous value to the ongoing development of all research team members and has led to new contributions to the field.

I**mpacts on knowledge translation and mobilization:** A manuscript has been submitted to *BMC Oral Health* and is currently under review. In addition, this work will be presented at the CIHR Institute of Cancer – CIHR Institute of Genetics New PI Meeting in Halifax, NS, Nov 2 – 4, 2022.

Impact on the team's abilty to secure additional funding: Support for this project has provided pilot data for submission to the following funding opportunities:

> <u>*Successful*</u>: Dalhousie Medical Research Foundation Health Research Excellence Grant. Early Career Investigator Award. The microbiome associated with oral epithelial dysplasia: a multi-omics study. (L. Rock [PI]); $35,000. (2022-2024). This project will expand on the above work by using a multikingdom approach to determine whether compositional and functional microbiome shifts associated with OED represent early events that correlate with the severity of dysplasia.
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> <u>*Submitted:*</u> NIH National Institute of Dental and Craniofacial Research, Funding Opportunity Announcement PA-20-185; *NOT-DE-21-015: The Functional Oral Microbiome* (submission date September 6, 2022; decision May 2023). The microbiome associated with oral leukoplakia: a multi-omics mechanistic study. (N. Al-Hebshi [PI]); $2.5M USD; Dalhousie site sub-award $393,433 USD. (2022 – 2027).

I would like to thank the Network for their unwavering support of oral health research and for making this research possible.

Sincerely,

Dr. Leigha Rock