# Supervisor & Project Information Form

Please complete and return via email ONLY to gdip.hres@utoronto.ca by *Monday September 30, 2019*

**Supervisor Information**

*MUST have unrestricted SGS appointment (appointment to supervise graduate students)*

<table>
<thead>
<tr>
<th>Name:</th>
<th>Email:</th>
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<tbody>
<tr>
<td>Douglas Chepeha</td>
<td><a href="mailto:douglas.chepeha@uhn.ca">douglas.chepeha@uhn.ca</a></td>
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<tr>
<th>SGS Department:</th>
<th>Field of Research:</th>
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<tr>
<td>Otolaryngology – Head and Neck Surgery</td>
<td>Cancer, Epidemiology, Tumor Microenvironment</td>
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<tr>
<th>Research Institution affiliation (if applicable):</th>
<th>Location of Work:</th>
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<tr>
<td>University Health Network Institute of Medical Science – University of Toronto</td>
<td>Toronto General Hospital</td>
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<th>Student contact time (number of hours per week YOU are available to the student for any concerns or to review progress):</th>
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<td>1 hour</td>
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**Title:** Mapping the Microbiome in Oral Cavity Squamous Cell Carcinoma

**Description (Max 500 Words):**

**Background**

The microbiome is important in other solid tumors particularly epithelial tumors of the gut. The oral cavity is part of the alimentary system and has not been extensively studied. It is reasonable to assume that the microbiome is important in head and neck carcinoma. Improved understanding of the microbiome may lead to prevention of squamous cell carcinoma (SCC), development of a prognostic factor or improve the efficacy of new adjuvant treatments. Additionally, there is recognition that there needs to be a greater understanding of the specific tumor and immune cell populations and their interaction (the invasive front/microenvironment).

The purpose of this project is to examine the microbial signature of oral cavity tumor and characterize the bacterial drivers that promote or inhibit an inflammatory response at the invasive front.

**Study population**

Patients with oral cavity squamous cell carcinoma, excluding lip and retromolar trigone, that will be treated with surgical excision.

**Study design**

Prospective study designed to examine the microbial signature of oral cavity tumor as well as evaluate the inflammatory response, EMT and cancer stemness at the tissue invasive front.

**Sample size**

The study will begin with 50 patients.

**Variables under study**

Identification of bacteria present in oral cavity and evaluation of differences in microbiome by patient disposition and survival outcomes. Established clinical and pathological staging of oral cavity cancer, grading of the invasive front, grade of inflammation, keratinization, cell nest distance and survival. New data elements include cellular components of the associated inflammatory response, and pattern EMT at the invasive front.
**Statistical Analysis**

Operational taxonomic units will be used to perform alpha (diversity within a sample) and beta (patterns of similarity and difference among samples) diversity calculations. Markers will be correlated to inflammatory response and to patient oncologic outcome. If correlated, then we will perform COX proportional hazard modelling to help understand if there are markers of T cell response, EMT, and cancer stemness that are significantly related to inflammatory response.

**Logistical Implementation**

This study is REB approved. 2-7 swabs will be collected from each patient at two different time points. The invasive front of tumor specimens from UHN laboratory medicine-pathology will be retrieved, photographed and graded per Bryne et al including the grading of the inflammatory response. The funding for this grant will support cutting slides of the invasive front and staining of cell populations in the inflammatory response in addition to markers of EMT, cancer stemness, and transcription factors. These slides will be photographed with Aperio imaging software at 40X and catalogued in the existing database. The head and neck pathology fellow who is supported by the head and neck translational program will assist in grading and describing the photomicrographs for analysis. There are 18 patients who have complete sets of microbiome samples and are undergoing analysis.

**Importance**

This project is designed to generate preliminary data for future grant support. There is strong statistical significance seen between inflammatory response and better outcome in a multivariate (Cox) model. It is important to note that these findings are from the tumor/host interface. This is an opportunity to examine the microbial signature or oral cavity tumor samples and the stability of the microbiome overtime. It will also expand the understanding of an aggressive tumor phenotype (EMT) and the inflammatory reaction.
Graduate Diploma in Health Research Program – 2020/2021

If human subjects are involved, have the appropriate Research Ethics Board approvals been obtained?
☑ Yes ☐ No ☐ Application Submitted (Date: ____________)

Do you expect this work will be published within the 20 months?
☑ Yes ☐ No ☐ Uncertain / Other
**Student Roles & Responsibilities (please be as specific as possible)**

**Clinical Role**

The student will be tasked with collecting participants’ data. The student will also assist with the collection of mucosal swabs from the participants, contribute to analysis of output and drive the manuscript preparation.

**Laboratory Role**

The student will assist with immunohistochemical staining. The tissue will be stained for markers of EMT, cancer stemness, and transcription factors. They also have the opportunity to work in the microbiome lab to process the isolates.

**Importance of Student’s Role**

The oral cavity microbiome and its role in oral cavity squamous cell carcinoma is not well understood or studied. Few studies of OCSCC have addressed the correlation of immunohistochemistry to the invasive front (IF). IF is a known clinical variable that is associated with more aggressive tumor characteristics. Understanding the molecular mechanisms contributing to a more aggressive IF should facilitate the investigation of targeted treatment and customization of care. This is a collaborative team project involving epidemiologists, pathologists, oncologists and basic science researchers. There will be presentation opportunities. Team publication is directly related to the student’s contribution to the research and willingness to write.
Please indicate who will serve as the student’s direct report for daily oversight (PI, PhD student, technician, etc...)

**Douglas B Chepeha,** MD, MScPH, is the principal supervisor. He will oversee all aspects of the project. He is a Full Professor at the University of Toronto and an Adjunct Professor at the University of Michigan in the Departments of Otolaryngology-Head & Neck Surgery. He is a member of the Institute of Medical Science and had a Masters of Science in Statistics and Research Design from the University of Michigan School of Public Health. He practices as a surgical oncologist and a microvascular reconstructive surgeon. One of his research interests is the tumor microenvironment and the invasive front. He will be the direct report for the student who will interact with him on a weekly basis.

**Bryan Coburn,** MD, PhD, is the co-investigator. He is a clinician-scientist in Infectious Diseases. One of his research foci is interaction between human microbiome and diseases. He will be involved in the identification of bacterial colonies in the swab samples.

**Carissa Thomas,** MD, PhD, will be a co-supervisor. She is an Assistant Professor at the University of Alabama at Birmingham in the Department of Otolaryngology. She practices as a surgical oncologist and a microvascular reconstructive surgeon. Her research interests and expertise lie in the interaction between microbiome and head and neck squamous cell carcinoma.

**Hedyeh Ziai,** MD – PGY3 Resident in the Department of Otolaryngology – Head & Neck Surgery, will work in concert with the student and provide direct supervision with day to day management of clinical data and annotating the immunohistochemical staining.

**Carolyn Barsoum,** BSc – Research Coordinator, will be responsible for data management and coordination of all meetings. She will be the administrative lead and help the student stay organized within the team.