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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**Project Information (will be posted on GDipHR website for student access)**

**TITLE:** Characterization of the Invasive Front in Oral Cavity Squamous Cell Carcinoma

**DESCRIPTION (MAX 500 WORDS):**

*Background*

The discovery of the H6B1 (PD-L1) receptor, has stimulated renewed enthusiasm for understanding the role of the immune system with respect to recognition of malignant tumors. Specifically, 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 evaluate the inflammatory response at the invasive front and to

*Study population*

Patients with Oral Cavity Carcinoma who have undergone treatment between 2005 and 2017 will be included in the cohort.

*Study design*

Retrospective correlative marker designed to evaluate the inflammatory response, EMT and cancer stemness at the invasive front along with oncologic outcomes.

*Sample size*

There are approximately 700 subjects in the dataset. A matched case series of 50 cases and 50 controls. A sample of 50 cases in each group will be able to detect a correlation of 0.2 to 0.99 with a beta = 0.2 and alpha = 0.05, two tailed.

*Variables under study*

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

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

The invasive front of specimens from UHN laboratory medicine-pathology have been 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.

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 expand the understanding of and aggressive tumor phenotype (EMT) the inflammatory reaction.
If human subjects are involved, have the appropriate Research Ethics Board approvals been obtained?
☒ Yes ☐ No ☒ Application Submitted (Date: 05 July 2019)

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 the collection of clinical data, contribute to analysis and drive 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. In addition, there is going to be evaluation of the differential importance of the cell versus the stroma. The IF and the cores will be photographed and catalogued in an existing database. In addition, the IHC grading and IF data will be added to the existing OCSCC database.

Importance of Student’s Role

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 long-standing collaborative team project. There are epidemiologists, pathologists, oncologists and basic science researchers who are involved. 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 has 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.

**Ben Wang**, PhD, is the lab supervisor. He will mentor and assist with interpretation of the tumor microenvironment. He works in the Pam Oashi lab at UHN where transformative research is taking place with respect to T cell response and treatment in solid tumors.

**Carolyn Barsoum**, MSc – 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.