Graduate Diploma in Health Research PROGRAM – 2018 SUPERVISOR & PROJECT INFORMATION FORM

Please complete and return via email only (gdip.hres@utoronto.ca) by ***September 4, 2018***
(forms received after this date will not be posted).

Supervisor Information

Name: Douglas Chepeha

Email: douglas.chepeha@uhn.ca

Degree(s): MD, MScPH, FACS, FRCS (C)

SGS Department: Otolaryngology – Head and Neck Surgery

Academic Rank: Professor

Field of Research: Cancer, Epidemiology, Tumor Microenvironment

Research Institution Affiliation (if applicable):

University Health Network
Institute of Medical Science – University of Toronto

Allocation of student contact time: 1 hour
(number of hours per week YOU are available to the student for any concerns or to review progress)

Project Information (for posting on GDipHR website)

Title: Evaluation of the Peri-Tumoral Inflammatory Microenvironment for Patients with 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 determine if there is a relationship to a more aggressive tumor phenotype, EMT.

Study population

Patients with Oral Cavity Carcinoma who have undergone treatment between January 2007 and January 2018 are included in the cohort. A well characterized population of 300 patients from 2007-2014 has undergone extensive analysis, tissue microarray assembly and preliminary immunohistochemistry.

Study Design

Retrospective correlative molecular marker designed to evaluate the inflammatory response and EMT at the invasive front.

Sample size

A sample of 300 cases will be able to detect a correlation of .2 to .99 with a β=0.1 and α=0.01, 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 will perform cox proportional hazard modeling to help understand if there are markers of EMT that significantly related to the inflammatory response.

Logistics of Implementation

This study has been REB approved. 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 (e-cadherin, n-cadherin vimentin), cancer stemness (CD44), and transcription factors (snail, slug, twist1). 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 ☐N/A

Do you expect this work will be published within the 20 months?
☑YES ☐NO ☐Uncertain

Student's roles and responsibilities (please be as specific as possible):

Clinical Role

300 Oral Cavity Squamous Cell Carcinoma (OSCC) resection specimens have been aggregated from a cohort of patients who underwent surgery from 2007-2014. The student will be tasked with updating the clinical data for this patient population from 2014-2017. This update will add another 390 patients.

Laboratory Role

The student will assist with immunohistochemical staining. The tissue will be sequentially stained for markers of EMT (e-cadherin, n-cadherin vimentin), cancer stemness (CD44), and transcription factors (snail, slug, twist1). 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 the database. In addition, the IHC grading and IF data will be added to the existing OCSCC database.

Importance of the 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 had a Masters of Science in Statistics and Research Design from the School of Public Health. He practices as a surgical oncologist and a micorvascular 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.

Laurie Ailles, PhD, will be a co-supervisor. She is an Investigator II at OICR, a member of the head and neck oncology program and co-characterized the first head and neck stem cells. She is collaborator with STARR and will be involved in the immunohistochemical staining of the tumor samples.

Neil Verma, MDCM, MSc – PGY2 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 immunhistochemical staining.

Feben Alemu, 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.