

University of Missouri South African Educational Program (UMSAEP) 2023 Partnership Grant Report

UMSAEP Visitor : Professor Henry A. Adeola (UWC)

Hosted by: Professor James K. Bashkin

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Background

Oral head and neck cancer (OHNC) burden is very high in Africa and there are limited multimodal tools for broad-based biomonitoring, detection, prevention, and risk stratification on the continent. Socioeconomic, geographical, linguistic, and political factors, inter alia, have posed barriers to oral health care access in Africa. The World Health Organization identified good oral health as a crucial component of overall health and wellbeing, and systemic diseases may present with diagnostic clues. Risk factors such as tobacco smoking, infectious agents, unhealthy (sugary/fatty) diet and lifestyle, as well as alcohol consumption

Africa regions. Hence, our team (comprising of investigators from University of Cape Town (UCT) University of the Western Cape (UWC) in South Africa, and University of Missouri, USA (UM)), planned to establish and sustain a multidisciplinary HPV-OHNC project through the UM/UWC Linkage Program to develop innovative in-silico data science tools for prompt detection of HPV+ OHNC in African patients.

2. Investigative Team Architecture

We assembled a team of clinician-scientists, basic scientists, bioinformaticians and data scientists 4.2 (s)-8.204.

- (b) Real-time PCR analysis of saliva samples for high-risk HPV-related DNA fingerprints in prospectively collected saliva samples.
- (c) Integrate both data to develop a multimodal diagnostic algorithm.

5. Achievements

(i) Pre-visit Activities: The first virtual meeting was initiated by Professor Rodney Uphoff, who is the Director of the UMSAEP program. This meeting was used to establish linkage between the 2 universities and to discuss the projects. Thereafter, several zoom meetings were held between the UWC and UMSL teams to discuss the project logistics and work strands that will be achieved during the visits and those that will be ongoing beyond the visit. Fortunately, our project was considered positively by the UMSAEP, and this grant solidified our bilateral interaction. The first task that we took on before the UMSL visit was to jointly write a U01 National Institute of Health (NIH) Grant. The DS-I Africa U01 is a flagship grant for data science for health discovery and innovation in Africa and it is funded through the Fogarty international NIH initiative. It is captioned “Harnessing data science technologies to develop solutions to the continent's most pressing public health problems”. Towards the funding call, our team proposed a project entitled “Developing a multimodal, integrative, in-silico, multiomics data science approach to early detection of HPV-based biomarkers of oropharyngeal head and neck cancer”. Although the project was not sanctioned by the NIH, it was

immunomodulatory role of tumor-infiltrating lymphocytes (TILs) and tumor-associated macrophages (TAMs) in the microenvironment of HPV+ OHNC. This broadened the scope of the project and strengthened a trilateral collaboration between USA, Africa, and Europe. The tripartite collaboration was invited to present our collaborative project at the UMSAEP precision medicine conference at UWC between March 27-April 1, 2023. Our UM-UWC project was also selected for presentation at the conference.

(ii) Activities during the trip: The visit focused mostly on aspects on objective (a) due to the short duration of the trip. In collaboration with a graduate student (Ms. Jessica Thompson), we tried to identify an in-silico peptidomimetic inhibitor target for the HPV viral oncoprotein E6 ubiquitin ligase domain (E6AP). In silico inhibitors were screened from synthetic and natural compounds and synthetically modified to increase binding affinity for the E6AP domain. Among natural compounds found were Ginkgetin, Hypericin and Apigetrin, while synthetic compounds included (S)-N-((3-amino-1-(5-ethyl-7H-pyrrolo [2,3-d]pyrimidin-4-yl)pyrrolidin-3-yl)methyl)-2,4-difluorobenzamide, dihydroxyphenyl)methylidene]-7-hydroxy-4-oxochromen-5-yl] acetate), N-((6-methyl-1H-benzo[d]imidazol-2-yl)methyl)-5-(thiophen-2-yl)-1H-pyrazole-3-carboxamide, and N1-(5-chloro-2-cyanophenyl)-N2-(2-hydroxy-2-(1-methyl-1H-indol-3-yl) ethyl) oxalamide. Work is still ongoing to optimize a natural flavonoid compound and a syntheu0.6 (3.1 (hy)-.2 ((d)-0.c(s)).

he had a mini-workshop with the students to teach them the principles of mass spectrometry and high performance liquid chromatography. He assisted graduate students with their research and participated in ongoing synthetic chemistry of

The visit period to UMSL was used to fine-tune the oral presentation of the HPV-OHNC project by Professors Adeola and Bashkin at the Precision Medicine Conference at the University of the Western Cape, upon their return to Cape Town, South Africa.

(iii) Post-visit activities: Both Professors Bashkin and Adeola travelled back to South Africa and arrived in Cape Town on Saturday 25th March 2023, ahead of the precision medicine conference. They attended the opening dinner on the 26th of March and presented their work at the precision medicine conference on Tuesday 28th March 2023. The conference was used for networking local within UWC and with other colleagues from Ghent University and the University of Missouri SystC /LBo.6 (u)8 (t)

microenvironment. The proposed study aims to evaluate the prevalence of HPV in a more heterogeneous population of otss-0.6 (es-0.6 ()8.6 (t)r)7C6 ()3 (P)rite