

University of Missouri - University of the Western Cape

Academic Exchange Programme for 2021

Report

Precision Medicine: Radiogenomics and Development of Individualized Radiation Therapy for Cancer

Visit to Columbia (Missouri) from 02 November 2021 to 29 November 2021

Submitted by Prof Mongi Benjeddou
Department of Biotechnology, University of the Western Cape

UM Host: Dr Gregory B. Biedermann
Department of Radiology, University of Missouri, Columbia, MO.

1. Background

The purpose of this UM-UWC academic exchange application was to request funding to make a research visit by Prof M Benjeddou (UWC) to the University of Missouri-Columbia from 6 September to 5 October 2021, as part of the collaboration project with Dr G Biedermann (UM). The collaborative project is entitled “**Precision Medicine: Radiogenomics and Development of Individualized Radiation Therapy for Cancer**”, and aims to develop and validate individualized radiation therapies for cancer patients.

Radiotherapy is a commonly used treatment modality for various solid tumors. Radiation exposure, however, often results in toxicity that compromises organ function and affects the quality of life for many cancer survivors. Although radiotherapy is primarily a local treatment, patients are exposed to a risk of toxicities in the treatment field and surrounding tissues, which may develop acutely and late.

There is a large patient-to-patient variability for the development of adverse reactions following radiotherapy, in terms of both prevalence and severity. The known causes of variation in incidence or severity of toxicity include radiotherapy dose, dose distribution, co-morbidities such as diabetes, concurrent chemotherapy, as well as genetic factors in the form of SNPs or other genetic alterations such as copy number variants

2. Description of activities during the visit

The joint research project is set take full advantage of opportunities within the University of Missouri's new \$220 Million initiative focused on Precision Medicine. The project brings together two research teams with extensive and complementing expertise. Prof Benjeddou's research team is multidisciplinary, and has extensive expertise in molecular biology, genetics and clinical work. It has made a clear contribution in the development and implementation of precision medicine for indigenous and admixed populations from South Africa. An extensive amount of important pharmacogenomics data has been generated for these populations. Dr Biedermann's research team has a lot of experience with head and neck cancer patients, and has focused on radiation therapy technology improvements, and quality of life including toxicity reduction as primary focus of clinical research. Researchers and postgraduate students will be spending time in each other's lab to gain valuable training and acquire valuable skills for the benefit of the project.

The following are the main activities of Prof Benjeddou's during his research visit to the Department of Radiology in the School of Medicine at the University of Missouri, Columbia, MO:

- Samantha Cairncross (PhD student; awarded funding from the University of Missouri South African Education Program) and Sheridan Llyod (M.Sc student; awarded Henry Mitchell Scholar) visited Biedermann's lab, where they spent 6 weeks and were involved in the setting up of the various assays to process samples collected from patients, as well as the preparation of the IRB's application.

- Before commencing with research at UM, Samantha and Shridon completed the CITI (Collaborative Institutional Training Initiative) biomedical training course. CITI training is intended for anyone involved in research studies with human subjects, or who have responsibilities for setting policies and procedures with respect to such research, including Institutional Review Boards (IRBs)

- An expedited IRB application was submitted and approved for the project (IRB #2069706).

- Subsequent to the IRB approval of the project's research protocols, 4 patients were enrolled, with blood drawn, processed, and irradiated. Radiation-induced lymphocyte apoptosis (RILA) assay was performed on the irradiated samples, as part of the research aimed at developing assays to predict patients most likely to experience severe toxicities following radiotherapy for cancer patients.

- Regarding the students' visit to UM, Dr Biedermann wrote: "I want to let you know what a pleasure it was to work with Samantha and Sheridan. From working through the steps, to getting everything set up in this project they made such a positive impression on everyone they interacted with."

- During the first week of Prof Benjeddou's visit to UM, he also completed the CITI (Collaborative Institutional Training Initiative) biomedical training course. Thereafter, he met with Dr Biederman to review all aspects of the project, which included the data collected from the patients enrolled thus far.

- Meeting with the Chair of the Radiology Department:

Prof Benjeddou met with Dr Talissa Altes, the Chair of the Department of Radiology, together with the Dr Biedermann and senior members of his research team. An update on the progress in the collaboration and the research project was presented in the meeting. Ways to support the project was discussed with the Chair of the Department of Radiology.

- Meeting with the Associate Dean for Population Health & Outcomes Research

Prof Benjeddou met with Prof Gillian Bartlett-Esquilant, Associate Dean for Population Health & Outcomes Research and Co-Director of the Translational Biosciences. The current concentration of Dr Bartlett-Esquilant is on knowledge translation and stakeholder engagement around health care utilization and outcomes for vulnerable populations; implementation of precision medicine using patient-oriented strategies. The implementation of precision medicine with a special focus on vulnerable and disadvantaged population groups was identified as common research area of mutual interest and future collaborations. Prof Bartlett-Esquilant will be visiting Cape Town (South Africa) in July 2022, as part of an existing collaboration with other colleagues from UWC. A follow up meeting is scheduled with Dr Bartlett-Esquilant during her visit to Cape Town to discuss progress in the proposed collaboration.

- Meeting with the Associate Dean for Clinical Translational Research

Dr Parvesh Kumar is a radiation oncologist and the Associate Dean for Clinical Translational Research at UM. In this meeting, the aims and the objectives of the radiogenomics were explained to Dr Kumar, as well as the specific areas where support is needed. He has expressed his support for the project, and promised to assist in many ways, including research grant applications within UM and other national funding institutions.

- Meeting with the Senior Associate Dean for Research, School of Medicine

Dr William P. Fay, the Senior Associate Dean for Research in the School of Medicine at UM, has given his full support to the project from the very beginning. The support included, among others, a small grant to help in lab running costs during the students' visit, and regular follow up on progress. The meeting was an opportunity to highlight the strengths of the collaboration and the great potential of

research project to Dr Fay. The main challenges and needs for the project were discussed with Dr Fay, which included the following:

1. Basic science researcher in either Radiobiology or Genomics needs to be identified or recruited at UM. This is by far the greatest gap and need identified here.
2. Lab space for blood processing, assays, DNA extraction for the samples. Space in the NexGen building, or space with the lab of an identified basic researcher whether they exist or are recruited.
3. Potential need for large-scale genotyping analysis. Potential solutions already exist.

- Meeting with the Director of the Bioinformatics and Analytics Core

A meeting was held with Dr Lyndon M. Coghill, the Director of Bioinformatics and Analytics Core at UM. He has expressed his willingness to collaborate in the project and assist in the bioinformatics analysis.

- Meeting with the Director of the Genomics Technology Core

Prof Benjeddou met with Dr Nathan Bivens, the Director, Genomics Technology Core. Dr Bivens confirmed that the genomics core is in a position to assist in the sequencing and genotyping. His group can offer two sequencing based approaches to genotyping. The first is whole genome sequencing which will generate 20-30x coverage per sample. The other approach is a target amplicon approach using primer panels for specific genes/regions of the genome.

- Meeting with the Associate Dean and the Director of Research and Graduate Studies at UMKC School of Pharmacy

The meeting with Dr Roger Sommi (Associate Dean and Professor at UMKC School of Pharmacy) and Dr Gerald J. Wyckoff (Director of Research and Graduate Studies, UMKC School of Pharmacy) was done via Zoom. In this meeting, Prof Benjeddou explained the aims and the objectives of the radiogenomics, highlighted the specific areas where support is needed, as well as the great potential for collaboration.

Dr Wyckoff has agreed to "champion" the wet lab work and the processing of samples including the logistics around collecting/shipping of samples, as well as the processing of samples, and performing the cell-based and DNA-based assays. This includes possible recruitment of a research assistant for a start, and finding space to create a genetics and molecular biology wet lab. He also might be able to provide some funding for a postdoc from Benjeddou's group, Dr Keenau Pearce, to come to MU in March/April/May for a month to help in the lab work. He will also be able to contribute in the writing up of grant proposals. As he has existing collaborations with UWC, he will be visiting Cape Town in June/July.

I am pleased to report that Dr Keenau Pearce has been awarded funding for a month-long research visit to Kansas City as part of the UMSAEP UMKC/UWC Data Analytics Training in Health Sciences Fellowship Program.

- Meeting with the Director of UM Cancer Nanotechnology Platform

The meeting with Dr Kattesh V Katti (Director of UM Cancer Nanotechnology Platform) was an opportunity to discuss possible collaborations in cancer research between Benjeddou's group and the UM Cancer Nanotechnology Platform. An area of common interest was identified, which was the development of innovative theranostic tumor-specific gold nanoparticles and the corresponding radioactive gold nanomaterials from Au-198 and Au-199 isotopes.

Back in South Africa, and as a follow up, Prof Benjeddou has had a meeting with the Director of iThemba LABS, Dr FAÏÇAL AZAÏEZ to explore the possibility of collaboration and using their facilities to manufacture the necessary radiopharmaceuticals and radiochemicals to be used in the UM-UWC collaborative research (<https://tlabs.ac.za/nuclear-medicine/radiopharmaceutical-and-radiochemicals-manufacturing/>). He has given his full support, and advised to work with his radiobiologist, Dr Charlot van der Voorde, to submit a research proposal, which must include research needs in terms of infrastructure and equipment.

- Other Meetings and Activities:

- One of the highlights of the visit to UM was attending 2 football games and 2 basketball games. Tickets were kindly provided by Prof Rod Uphoff.
 - In the first football match, I met with Dr Mun Y. Choi, the University of Missouri President, Dr Latha Ramchand, the UM Provost and Executive Vice Chancellor for Academic Affairs and Dr Richard Barohn, the UM Executive Vice Chancellor for Health Affairs.
 - Dr Barohn followed up on our conversation around the project, connected me to Dr Kumar for further assistance as mentioned above, and he is still in contact with Dr Fay and Dr Biedermann to follow up on progress.
- Meeting with Dr Jeffrey Whyte, Senior Researcher in Laboratory for Infectious Disease Research. Assistance with cell-based assays were discussed, including the use of the lab instruments.
- Meeting with Dr Lee-Ann Allen, Chair of Department of Molecular Microbiology & Immunology. The meeting was a follow up on the discussion with Dr Whyte regarding the use of the research facilities in the department to perform some of the assays, and provide some support for the lab work in general.
- Meeting with Dr. Guangfu Li (Department of Molecular Microbiology & Immunology). The meeting was an opportunity to thank Dr Li for kindly hosting Samantha and Sheridan in his lab during their visit to UM, and assisting them in performing their lab experiments and assays.

3. Conclusion

I would like to thank all colleagues for making the time to meet and discuss ways to support our research project, as part of MU-UWC research collaboration programme. Looking forward to working with all on this exciting project in the area of precision medicine/oncology and pharmaco/radiogenomics. The project has a great potential in the UM NextGen and Precision Health aims.

I am very excited about the future of this collaboration project, and already looking forward to my next trip to Missouri!!

4. Acknowledgments

I would like to thank Prof Rod Uphoff for the excellent support he has provided me and my students.

Thank you Rod and Marsha for inviting me over, together with other UWC colleagues, to have an great dinner just before leaving for Thanksgiving.

Name: Prof Mongi Benjeddou

Date: 26/02/2022

Signature:

