

UMKC/UWC Data Analytics Training in Health Sciences Fellowship Program

UMSAEP 2022 REPORT

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Abstract from proposal:

Our partnership seeks to increase the capacity for data science research and innovation in the health and life sciences in Africa by supporting trainees from the University of the Western Cape (UWC) in a robust training environment within the University of Missouri-Kansas City (UMKC). As a capacity building proposal, the goal is to offer opportunities to UWC scholars to enable them to become the next generation of research leaders for collaborative work. By establishing a visiting scholar program between UWC and UMKC centering around our shared schools of Pharmacy, we will address deficiencies in a submitted DS-I Africa training proposal which will allow us to be successful with a subsequent submission. There have been numerous examples of successful collaborations across the nearly 30-year history of this partnership- at UMKC, some highly relevant examples include the UMKC Mathematics and Statistics department hosting UWC investigators, as well as teaching a numerical analysis course at UWC; Dentistry hosting several visiting scholars; and current joint grant development efforts between UMKC and UWC Pharmacy schools as well as engagement between the Bloch School. We seek to build a more formal exchange of scholars on a short-term, regular basis to address challenging problems in health data analytics.

Overall, the goal was to have four UWC scholars visit UMKC, and Dr. Wyckoff visit UWC, in order to develop new opportunities for fundable research.

Proposed outcomes:

- 1) Each student will be expected to submit at least one paper on work that was produced, in whole or in part, during the collaborative period funded by this work.
- 2) Each student will be expected to graduate within 12 to 14 months from participation in this program.
- 3) At the conclusion of the program, a seminar will be held at UWC to highlight the work performed by the students during the collaboration.
- 4) At least one faculty member who can champion a U2R submission focused on data analysis in health sciences at UWC will be identified at the end of this project.
- 5) Creation of the "Visiting Scholars" program

Adjustments:

Due to some ongoing Visa delays, as well as match of scholars and projects, three out of four of the scholars supported were more senior and had already achieved their PhD. Therefore, the metric of graduation within 18 months was not applicable. However, these scholars were asked to develop new projects that could be fundable from their work at UMKC.

Travel Activities:

Four scholars from UWC visited UMKC:

Samson Oselusi (Jan 29-Feb 21, 2022)

Imaan Roomaney (March 3 -March 27, 2022)

Johan Breytenbach (Apr 6- Apr 30, 2022)

Keanu Pearce (May 1 – May 26, 2022)

Additionally, prior to the start of the grant Dr. Wyckoff hosted Luke Zondagh to work with Dr. Bill Gutheil at UMKC School of Pharmacy (July 30-August 7, 2021)

All of the scholars were housed at Diastole, across the street from UMKC's Hospital Hill; Luke Zondagh was hosted at a local hotel.

Oselusi: As part of the Oselusi visit, a paper was produced
Oselusi, S. O., Fadaka, A. O., Wyckoff, G. J., & Egieyeh, S. A. (2022). Computational Target-Based Screening of Anti-MRSA Natural Products Reveals Potential Multitarget Mechanisms of Action through Peptidoglycan Synthesis Proteins. *ACS omega*, 7(42), 37896-37906.

This abstract from this paper is in the appendix of this report.

Mr. Oselusi was predominantly working in the Wyckoff lab, but also spent time working within the Mass Spec facility at UMKC working with students from Dr. Gutheil's lab. The focus of this work was to extend his research from computational results on drug screening into bench assays for drug candidate effectiveness.

Dr. Roomaney worked within the Wyckoff lab to extend her range of laboratory techniques, and met with several UMKC School of Dentistry faculty to discuss potential collaborations. Additionally, we discussed how UMKC courses in biostatistics as well as other courses in data analysis may be useful for scholars such as Dr. Roomaney for extending her interest in dentistry and public health. One consequence of this was that Dr. Roomaney will be utilizing the UWC implementation of RedCap in her future work, and is likely to be in collaboration with a larger group of researchers at UWC in the future.

Dr. Breytenbach worked within the Wyckoff lab, primarily with Ms. Lauren Harrell and Mr. Drinnan Sante, both graduate students. One outcome from this research is a tool that Ms. Harrell is currently utilizing for natural language processing of her rare disease data; a paper is in process and an application for funding will proceed after the paper has been submitted. However, one of Dr. Breytenbach's meetings was with UMKC School of Pharmacy faculty member Dr. Mark Patterson, who is part of the Hi-IQ consortium at UMKC (working with Dr. John Spertus at St. Lukes) Dr. Patterson is an implementation specialist and works in health care

data analysis. Dr. Breytenbach produced a proposal for a pilot project which is now an ongoing collaboration between Drs. Breytenbach and Patterson- the abstract from the draft is attached as an appendix to the report.

Dr. Pearce and Dr. Wyckoff worked to determine the potential for performing pharmacogenomic analysis at UMKC, which would extend the reach of work that Dr. Mongi Benjeddou at UWC is currently performing. We were able to replicate the necessary resources for much of the project, but were unable to locate the appropriate radiation source either at UMKC or at UM Columbia for the project. We are still working to find this necessary tool. However, while at UMKC, Dr. Pearce, Mr. Sante, and Ms. Shivani Gargvanshi (a current UMKC Graduate student) worked to determine the feasibility of nanopore sequencing for pharmacogenomics projects both here and at UWC. The proposed platform is cost-effective and rapid, which meant that it could have provided more screening capacity at UWC. However, the ultimate outcome of the work suggests that the nanopore sequencing technology is too fragile to serve as a robust pharmacogenomics screening platform for Dr. Benjeddou's studies. That we were able to quickly develop, troubleshoot, and dis-regard the technology at UMKC advanced the work that Dr. Pearce is currently engaged in at UWC.

Pictures from UMKC Scholar Visits:



Dr. Wyckoff Visited UWC

June 4- June 21, 2022

Dr. Wyckoff travelled to Cape Town and had approximately 16 meetings in his approximately 14 days visiting UWC.

Individuals within these meetings:

Samson Oselusi <https://www.researchgate.net/profile/Samson-Oselusi>

Johan Breytenbach <https://za.linkedin.com/in/johan-breytenbach-phd-03672917>

Imaan Roomaney <https://za.linkedin.com/in/imaan-roomaney-43751753>

Luke Zondagh <https://www.researchgate.net/profile/Luke-Zondagh>

Keenau Pearce <https://za.linkedin.com/in/keenau-pearce-16677a10a>

Anthea Rhoda <https://za.linkedin.com/in/anthea-rhoda-61088733>

Mattia Vaccari <https://astro.uwc.ac.za/mattia-vaccari/> (now at University of Cape Town)

Mongi Benjeddou <https://scholar.google.co.za/citations?user=KylzO2IAAAAJ&hl=en>
Jose Frantz <https://za.linkedin.com/in/jose-frantz-29188633>
Umesh Bawa <https://international.uwc.ac.za/about/team/mr-umesh-bawa/>
Julie Philips <https://physio.uwc.ac.za/staff/julie-philips/>
Asha George <https://soph.uwc.ac.za/school-of-public-health/staff/professors/prof-asha-george/>
Ana Casanueva <https://www.astp4kt.eu/about-us/ana-casanueva.html>
Thabile Sokupa <https://www.researchgate.net/profile/Thabile-Sokupa>
Samuel Egieyeh <https://scholar.google.com/citations?user=wDKTnmcAAAAJ&hl=en>
Nicole Keuler <https://za.linkedin.com/in/nicole-keuler-6ba397131>
Kenechukwu Obikeze <https://scholar.google.com/citations?user=JAEtjh4AAAAJ&hl=en>
Jacques Joubert <https://www.researchgate.net/profile/Jacques-Joubert-2>
Afeez Kareem <https://www.researchgate.net/profile/Afeez-Kareem>
Erika Kapp <https://za.linkedin.com/in/erika-kapp-4a47b722>
Sarel Malan <https://scholar.google.com/citations?user=UXfitAwAAAAJ&hl=en>
Admire Dube <https://scholar.google.com/citations?user=6aBQi0EAAAAJ&hl=en>
Elizabeth Egieyeh <https://za.linkedin.com/in/elizabeth-egieyeh-05b5b982>
Denzil Beukes <https://scholar.google.co.za/citations?user=7P6i28UAAAAJ&hl=en>
Veerasamy “Jeff” Yengopal <https://www.uwc.ac.za/news-and-announcements/announcements/new-dean-of-dentistry-appointed>
David Fisher <https://www.researchgate.net/profile/David-Fisher-10>
Khayelihle Brian Makhathini <https://scholar.google.co.za/citations?user=OsgYjV0AAAAJ&hl=en>
Larry Pokpas <https://www.usaf.ac.za/wp-content/uploads/2021/09/Mr-Larry-Pokpas-Abridged-Biography.pdf>
Eslam Hussein <https://scholar.google.com/citations?user=cGvZICkAAAAJ&hl=en>
Frederic Isingizwe <https://eresearch.uwc.ac.za/2020/11/19/welcome-to-dr-frederic-isingizwe/>
Carolina Odman <https://www.google.com/search?client=firefox-b-1-d&q=Carolina+Odman+UWC> (now deceased)
Burtram “Bertie” Fielding https://www.ws-virology.org/dt_team/burtram-fielding/

Since returning, I’ve also discussed opportunities with:

Anita Burger <https://imbm.co.za/staff/dr-anita-louize-burger/>
Jennifer Chipps <http://repository.uwc.ac.za/xmlui/handle/10566/1657>

As part of my time at UWC, I gave a seminar for the CHS faculty on Friday, June 17th entitled “Considerations on the use of machine learning for health science applications; Pharmacovigilance, Cancer Screening, and beyond.” I have enclosed the flyer from this in the appendix and can make the slides available to anyone interested.

Opportunities uncovered from these activities

While at UWC I met with several different faculty groups- all are extremely willing to collaborate with UM, as they see multiple opportunities to build on their international

(including NIH) funding with us as partners. One example of this is the work already being carried out between Dr. Anita Burger (UWC) and Dr. Kun Cheng (UMKC) for isolation of a biosurfactant with high potential for commercialization. Another is the work between Dr. Jacques Joubert (UWC) and Dr. William Gutheil (UMKC) isolating compounds with antibiotic properties. Dr. Admire Dube at UWC is R01 funded in immune modulation and looking for potential partners within the UM System. Dr. David Fisher at UWC has proposed significant collaborative work at UM. Other collaborations are ongoing, and there is a high potential for future work particularly in the following areas:

1) Compound Development and Delivery

UWC is home to several researchers who isolate and screen novel compounds derived from plants and marine organisms in Africa and specifically within the novel flora and off-shore environment of the Cape. These compounds represent novel scaffolds that are unavailable elsewhere. This represents an opportunity for access to these materials for joint development opportunities that could otherwise not be approached. This opportunity is well suited to the development of novel antibiotics; a key enabling technology for treatment particularly with MRSA and other resistant strains of bacteria on the rise in the US, South Africa, and globally.

2) Genome Wide Association Studies/Genomics/Clinical Trials

Because of its history, South Africa is a truly multicultural society that contains a wide set of genetic diversity- in many ways, this is similar to the large and diverse population of the United States. From the perspective of precision medicine, pharmacogenomics, and genome-wide analysis, studies that could utilize patient populations from the US and South Africa likely have more power to isolate genetic variants that are causal of or protective against disease states, or that alter drug distribution or response. Thus, collaborations with UWC researchers could enable more highly powered studies.

3) Digital Health Development

UWC has a set of researchers that are pursuing digital health solutions for patient access and treatment monitoring, and this mirrors interests and capabilities in the UM System. Notably, while the health care systems in the Cape and in the States are quite different, many of the problems faced (rural care, health disparities, drug abuse in patient populations, transitions of care) faced are the same across the groups. Therefore, applications- including machine learning and algorithm development- may be tested and deployed in multiple sites, leading to better outcomes with digital health platforms.

4) Clinical Trials

As noted above, the population structure of South Africa allows more highly powered studies from a genomics perspective. This may extend to potential clinical trials, should relationships with UWC develop sufficiently. Such trials would benefit from the community integration of UWC within the Cape.

5) Immune Modulation; Cancer therapeutics/Infectious Disease

Several researchers at UWC work in the area of immune modulation- this is a very large area of potential growth for precision medicine as such work will enable patients to fight off infections as well as cancer with the right immune modulation. This is an active area of research for several groups across the UM system with active funding and can be

utilized to enhance the amount of research, the number of grants applied for and received, and the relationship with UWC will enable potential more applications and a wider field of potential commercialization for such applications.

These opportunities are of course best pursued when there is mutual shared interest in the outcomes and potential grants available. Mutually beneficial projects will emerge which ultimately are funded and sustainable. Incorporation of these projects into the fabric of the Precision Medicine Institute will increase the reach of the institute, enable greater funding (enabling funding from sources such as the NIH DS-I program and others), and open access to more international partnerships and global commercialization opportunities.

An excellent opportunity for research funding was the new DS-I Africa grant cycle that launched at the NIH, and this allowed Dr. Wyckoff to discuss potential projects while at UWC given the deadline of an August 23rd LOI. That deadline was later adjusted.

RFA Link: <https://grants.nih.gov/grants/guide/rfa-files/RFA-RM-22-023.html>

Building on this grant opportunity and the likely commercialization and R01 grants that are being submitted will cement sustainable funding for future life and health sciences research focused on precision medicine within the UMSAEP collaborative framework.

By the end of this experience, a DS-I grant was submitted by the UWC group, with letters of support by Drs. Wyckoff and Uphoff, among others: "Africa-specific variants of Disease targets: An interactive platform and protein database for precision drug discovery, drug repurposing and biomarker development"

Luke Zondagh, Samuel Egeyah, Jacque Jouberts, and other UWC folks spearheaded the proposal and the UMSAEP supported experience was, I believe, crucial for the development of the grant.

Personal growth

I was very grateful to Dr. Rod Uphoff and his wife, Marsha, for their gracious effort to ensure my stay was productive and comfortable. As part of this, I was able to see a seminar by Albie Sachs (former South African Constitutional Court Justice), which was extremely interesting. I was also able to see some of the unique Fynbos flora in the western Cape, and see a troop of baboons up close; as close as anyone would safely want to get. As an evolutionary biologist, this was personally very meaningful for me. Having studied convergent and divergent evolution and having published on sexual selection in primates, I felt invigorated and privileged to see this. I also got to see two colonies of African penguins, which was quite special. I am now also able to use the word "lekker" properly in a sentence, and managed to have a proper Gatsby sandwich. I have included several pictures from my travels.



Ongoing Activities:

Collaboration between Drs. Egeyiah, Sun, and Wyckoff

Centered around drug screening

Biweekly meetings between Drs. Chipps and Wyckoff

Bringing in Iman Roomaney, Haly Holmes, and CHS personnel

Collaboration between Drs. Breytenbach and Patterson

Multiple grant opportunities, implementation science and data analysis

Continued Scholar exchanges are planned

Drs. Fisher, Joubert, Wyckoff

Our discussion noted that this would be an effective way to continue collaborations between the UWC and UMKC schools of Pharmacy, with an emphasis on shared infrastructure.

Computational Target-Based Screening of Anti-MRSA Natural Products Reveals Potential Multitarget Mechanisms of Action through Peptidoglycan Synthesis Proteins

Samson Olaitan Oselusi, Adewale Oluwaseun Fadaka, Gerald J. Wyckoff, and Samuel Ayodele Egieyeh*

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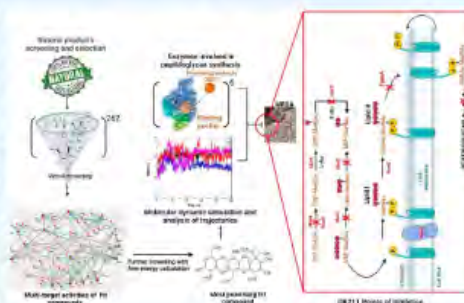
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ABSTRACT: Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the leading causes of bacterial infections in both healthcare and community settings. MRSA can acquire resistance to any current antibiotic, which has major implications for its current and future treatment options. As such, it is globally a major focus for infection control efforts. The mechanical rigidity provided by peptidoglycans in the bacteria cell walls makes it a promising target for broad-spectrum antibacterial drug discovery. The development of drugs that can target different stages of the synthesis of peptidoglycan in MRSA may compromise the integrity of its cell wall and consequently result in the rapid decline of diseases associated with this drug-resistant bacteria. The present study is aimed at screening natural products with known *in vitro* activities against MRSA to identify their potential to inhibit the proteins involved in the biosynthesis of the peptidoglycan cell wall. A total of 262 compounds were obtained when a literature survey was conducted on anti-MRSA natural products (AMNPs). Virtual screening of the AMNPs was performed against various proteins (targets) that are involved in the biosynthesis of the peptidoglycan (PPC) cell wall using Schrödinger software (release 2020–3) to determine their binding affinities. Nine AMNPs were identified as potential multitarget inhibitors against peptidoglycan biosynthesis proteins. Among these compounds, DB211 showed the strongest binding affinity and interactions with six protein targets, representing three stages of peptidoglycan biosynthesis, and thus was selected as the most promising compound. The MD simulation results for DB211 and its proteins indicated that the protein-ligand complexes were relatively stable over the simulation period of 100 ns. In conclusion, DB211 showed the potential to inhibit six proteins involved in the biosynthesis of the peptidoglycan cell wall in MRSA, thus reducing the chance of MRSA developing resistance to this compound. Therefore, DB211 provided a starting point for the design of new compounds that can inhibit multiple targets in the biosynthesis of the peptidoglycan layer in MRSA.



Appendix 2: Draft proposal abstract from Dr. Breytenbach

Implementing trained machine learning models for complication prediction in African preoperative settings

Johan Breytenbach*, Mark Patterson**

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Abstract

Purpose: Early evidence from sizeable US and African research shows that machine learning models can be trained to assist, with accuracy, in the preoperative identification of general surgery patients at risk of postoperative complications. Using the Implementation Research Logic Model (IRLM), an investigation is undertaken into the technical and non-technical determinants hindering the successful implementation of trained ML models into private and public preoperative settings in South Africa.

Methodology/design: First, a summative argument is presented from literature confirming that the technology and the data is available in Africa for training machine learning algorithms towards the identification of patients at risk of postoperative complications. The research question asks why such system implementations are not being undertaken, with a focus on barriers to implementation. Second, the study presents data from interviews conducted with information systems and medical experts involved in an exploratory five-year, early-technology-adoption project to implement ML models for complication prediction in two South African settings: (i) a private hospital, and (ii) a public hospital. Third, the presented interview data is enriched with comparative expert interviews from non-African experts from a Western setting with experience in the successful implementation of ML for complication prediction (MLCP) in the US. Fourth, using the IRLM framework as foundation, findings are presented, and suggestions made towards the successful implementation of MLCP in Africa.

Research limitations: This study used interview data from a single – the only available - longitudinal, well documented case study of an attempted implementation of MLCP in South Africa, with the case study spanning from 2018 and ongoing at time of publication. The data is thus only from South Africa, and describes a very early adoption of MLCP, which limits the generalizability of the findings. For this reason, the data was enriched using comparative insights from non-African experts into the research. Results are presented as practical implementation advice to information systems practitioners involved in MLCP and, whilst significant and valid, are yet to be validated in practice.

Practical implications: This research has implications for designers of systems that capture and use preoperative data. Important considerations for the implementation of MLCP in (i) private sector and (ii) public sector systems are presented, with examples.

Originality/value: This paper identifies key determinants and related resolution strategies for the implementation of MLCP in perioperative settings in Africa. The originality of our contribution resides in part in the focus on both private and public sector concerns around the implementation of MLCP in Africa, and in part in the presentation of findings within an accessible information systems implementation framework.



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