

2022 UMSAEP UM-UWC Academic Exchange Program Report

Anti-biofilm discovery and development using cheminformatic and biological approaches

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UM Host:

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1 Introduction

The University of Missouri (UM) System has had a partnership with the University of the Western Cape (UWC) for over 34 years. There have been over 900 faculty exchanges between the two universities and countless research collaborations across academic disciplines. Many of these collaborations have led to publications and external funding. Prof Rodney, Director of the University Missouri South African Education Program (UMSAEP), connected me with Prof. Sun, Department of Medicine, UM. In addition, he connected Dr Sun and I with UMKC's Dr. Jerry Wyckoff who is the Chair of the Division of Pharmacology and Pharmaceutical Sciences in the UMKC School of Pharmacy.

2 Collaborative Project

The collaborative project proposes to develop a novel platform to systematically analyze the extensive database of anti-biofilm agents to design novel anti-biofilm drug candidates with improved drug like properties which can be broadly applied to many diseases and pathogens.

3 Project Implementation

3.1 Activities prior to traveling to UM

In our previous studies at UWC, we have conducted scaffold diversity and comparison analysis of anti-plasmodial natural products, registered antimalarial drugs (CRAD) and malaria screen data from Medicine for Malaria Ventures (MMV). With regards to anti-biofilm compounds, initial cheminformatics profiling conducted on 350 compounds that have been reported to possess anti-biofilm properties revealed strategies that may be used for the design of novel anti-biofilm compounds. Molecular diversity exploration showed that the anti-biofilm compounds were mostly scattered within the chemical space with only one tight cluster, attesting to the moderate amount of molecular structural diversity of this anti-biofilm compound set. Molecular scaffold diversity of the compound set identified a total of 12 unique core scaffolds. We developed machine learning/deep learning classification models and pharmacophore models from anti-biofilm compounds. These anti-biofilm predictive models were used for data-driven decision making in the selection of potential novel compounds to be tested for anti-biofilm activities at UM. The selected compounds (5) were purchased from a chemical company in Ukraine and shipped to UM, Columbia campus.

3.2 Visit to UM

I travelled to Columbia, Missouri on Thursday, June 23 2022 through Frankfurt and arrival on Friday, June 24 2022. Friday, July 8 Saturday, July 9

3.3 Activities at UM

Evaluation of the anti-biofilm potential of the selected compounds

The synthesized compounds were tested in in-vitro biological functional assays that have been established in the preliminary studies within the lab of Prof Sun (Figure 1). A microtiter-based assays was used to measure the inhibition of *S. aureus* MRSA strain NRS384 biofilm formation. The efficacy of selected compounds (5) in the presence of human serum were determined by incubating bacteria with 50% human serum at 37°C with increasing concentrations of compounds to obtain serum IC₅₀. The result showed that compound 4 (Z56768216) is the best compound (Figure 2). Compound 1, 2, 3

also good activity, but there wasn't a clear dose-response and potency may need improvement. Compound 5 not very soluble.



Figure 1. The MU health care that houses the department of medicine. Prof Sun conducting *microtiter-based* anti-biofilm assays in her laboratory

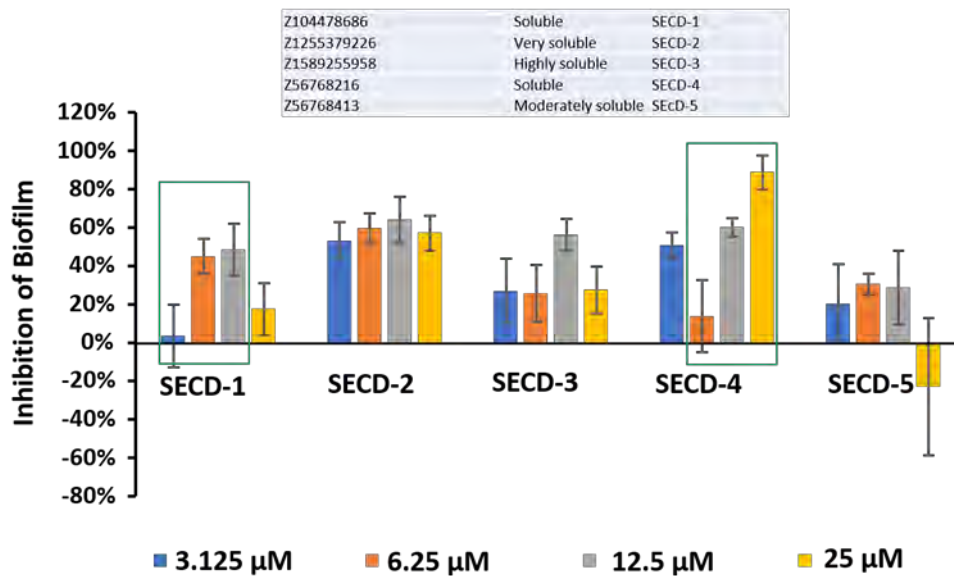


Figure 2. Biofilm formation inhibition by selected compounds at different concentrations.

4 Meetings and Facility Tours

1. I was taken on a tour of the Next Generation Precision Medicine facility (Figure 3) by the facility manager. I was blown away by the integrated laboratory structure that will house various research groups. The state-of-the-art microscopy facility was mind-blowing. I hope to explore this facility for future research.



Figure 3. Next Generation Precision Medicine Facility

2. I had an interesting meeting with Shyu Chi-Ren, the Director of MU Institute for Data Science and Informatics. We discussed the possibilities of a project around microbial evolution and drug discovery.
3. I had formal and informal meeting (Dinner) with Dr. Gillian Bartlett-Esquillant, the Associate Dean for Graduate Research Education. We discussed the possibilities for the implementation of research on precision medicine for mental health. Dr Gillian visited Cape Town the same week that I arrived back to Cape Town. We met once again and touched base with Prof Alan Christoffels of the South Africa National Bioinformatics Institute (Figure 4).



Figure 4. Prof Alan, Prof Gillian, Dr Kate and Dr Samuel at SANBI, UWC

4. I met with Joshi Trupti, the Director of the Health Management and Informatics unit. We discussed possibilities for research around collecting and analyzing complex genomic biological data for applications in medicine.
5. I made a presentation to the Department of Medicine on potentials for collaborations with my research group and other research groups in UWC

5 Outcomes

- Prof Sun, Prof Wyckoff and I submitted an NIH grant on anti-biofilm discovery and development using cheminformatic and biological approaches. Although we did not get the grant, we got a very useful feedback for the next round of submission.
- We have publication in collaboration with Prof Wyckoff: ACS Omega 2022, 7, 42, 37896–37906. Publication Date: October 14, 2022 <https://doi.org/10.1021/acsomega.2c05061>
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3.2 Return to UWC, Cape Town

I travelled back to *UWC, Cape Town* on Friday, July 8 and arrived on Saturday, July 9



