Contribution ID: **123** Type: **Poster (Chemistry SIG)**

Investigation of natural compounds for drug design; with analysis of structural variations of potential anti-stroke target, COX-1, due to associated non-synonymous SNPs.

BACKGROUND:
Stroke is the third leading cause of death worldwide, with 87% of cases being ischemic stroke. The two primary therapeutic strategies to reduce post-ischemic brain damage are cellular and vascular approaches. The vascular strategy aims to rapidly re-open obstructed blood vessels, while the cellular approach aims to interfere with the signalling pathways that facilitate neuron damage and death. However, according to the American Stroke Association, popular vascular treatments, such as tissue plasminogen activator (tPA), have been shown to have adverse side effects, including cerebral haemorrhage. This has necessitated the need for alternative chemotherapeutics.
Studies have shown that cyclooxygenase-1 (COX-1) plays a significant role in the post-ischemic neuro-inflammation and neuronal death. COX-1 is additionally irreversibly bound and inhibited by aspirin, another drug used to manage and treat stroke. These factors make COX-1 a plausible target for cellular treatment of stroke.
In this study, COX-1 is being investigated for identification of novel drug compounds and to assess the effect of nsSNPs on COX-1 structure and function.
METHODOLOGY AND RESULTS:
In a bid to discover novel drug compounds, ligands from the South African Natural Compounds Database (SANCDB - https://sancdb.rubi.ru.ac.za/) and ZINC database are being used for high-throughput virtual screening (HVTS) against COX-1. Additionally, five nsSNPs occurring in the COX-1 dimer interface are being investigated to assess their impact on protein structure and function. This computational work is being carried out on the NORMAL and SMP queues on the CHPC Lengau cluster. HVTS was conducted using Autodock Vina with GNU parallel, utilising a total 240 CPU cores running 12 jobs per node. The molecular dynamics for SNP analysis and molecular docking assessment is being run using Gromacs openmpi, utilising GROMOS96 54a7 force field, on 240CPU cores as well on the NORMAL queue. The molecular dynamics runs have been set for 100 ns, with an initial 10 ns run for all docked protein-ligand complexes to filter out undesirable protein-ligand interactions.
CONCLUSION:
Preliminary results include; a number of compounds showing favourable protein interactions within the cyclooxygenase active site of COX-1 and initial analysis of MD simulations indicates that some of the nsSNPs are affecting protein stability.

Presenter Biography

As a young female scientist , Ms. Tendai Muronzi believes science and innovation are the answer to solving a majority of issues Africa faces to date. Ms Muronzi is highly motivated in furthering her career and aims to change the face of science on the African continent. As a graduate of a BSc Hons in Biochemistry, she is currently studying as an MSc in Bioinfomatics student.

Primary authors: Prof. TASTAN BISHOP, Ozlem (Research Unit in Bioinformatics (RUBi), Department of Biochemistry and Microbiology, Rhodes University); Mr KIMUDA, Magambo Phillip (Research Unit in Bioinformatics (RUBi), Department of Biochemistry and Microbiology, Rhodes University); Ms MURONZI, Tendai (Research Unit in Bioinformatics (RUBi), Department of Biochemistry and Microbiology, Rhodes University)

Presenter: Ms MURONZI, Tendai (Research Unit in Bioinformatics (RUBi), Department of Biochemistry and Microbiology, Rhodes University)

Session Classification: Chemistry and Material Science SIG Seminar

Track Classification: Chemistry and Material Science SIG Seminar