Contribution ID: **14** Type: **Student Micro-talk**

Structural Bioinformatics Analysis of CYP2D6 pharmacogenetic variation relevant to Sub-Saharan African populations

Abstract:
Pharmacogenomics is a field of study that involves the association of genes involved in drug metabolism with drug response. The CYP2D6 gene is important for drug metabolism. Different studies have identified a number of variations in the CYP2D6 gene in African populations with potential functional impact. The aim was to gain insights of how missense variants found in sub-Saharan African populations may potentially impact the functionality of the CYP2D6 enzyme, with focus on a drug commonly used globally. Fifty missense variants identified in African populations were selected using the PharmVAR and GnomAD databases. Missense variants were prioritized for molecular dynamics using the Structural Workflow for Annotating ADME gene Targets (SWAAT) and the H3Africa dataset to identify variants that are more common in Africa and have a potential significant impact on drug metabolism. Missense variants which were exceptions to the prioritisation criterion were also selected for molecular dynamics assessments. The complex CYP2D6/thioridazines structure was used to run the molecular dynamics simulations as the reference structure and for the selected variants. A total of 10 missense variants were selected for molecular dynamics assessment. The study provides an insight of how missense variants may affect a protein at molecular level. The findings revealed the missense variants with potential significant effects on the enzyme's structure and potentially its functionality. These findings may be used to expand knowledge in pharmacogenomics which may be used to enhance precision medicine in Africa.

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Session Classification: Micro-talks

Track Classification: Bioinformatics and Biological Sciences