Potential drug targets in Mycobacterium tuberculosis through comparative genome analysis of three KZN strains.

Ruben Cloete¹, Ekow Oppon² and Alan Christoffels¹

 ¹ South African National Bioinformatics Institute, University of the Western Cape, Private bag-X17, Modderdam Road, Bellville, Cape Town, South Africa.
² Biomedical Informatics Research Division, eHealth Research Innovation Platform, Medical Research Council, P.O. Box 19070, Cape Town, South Africa, e-mail: ruben@sanbi.ac.za, ekow@sanbi.ac.za and alan@sanbi.ac.za.

It is estimated that one-third of the world population is infected with *Mycobacterium tuberculosis* (Mtb). However, only about 10% of infected individuals develop active TB during their lifetime. Despite having a variety of anti-tuberculous drugs, treatment options are often limited, due to the emergence of multi-drug (MDR) and extreme drug resistant (XDR) TB strains. This has prompted an urgent need of new drugs and the identification of new drug targets.

The sequencing and comparative analysis of the whole genomes of the three Tugela Ferry KwaZulu-Natal (KZN) (susceptible (DS), MDR and XDR) strains could provide valuable insight into Mtb pathogenicity.

We have downloaded the whole genome sequences from these three South Africa strains (XDR (KZN 605), MDR (KZN 1435), and DS (KZN 4207)) and identified drug resistance metabolic pathways of first and second-line anti-TB drugs. Novel drug targets in these metabolic pathways have been investigated and certain drug targets have been identified and six genes have been selected. Gene selection was based on information from text mining, essential for the growth of the organism, gene's function, uniqueness to Mtb and/or presence/absence of gene in the human host and finally degree of conservation amongst *Mycobacterium* species. We report on our drug target selection protocol and results of homology modelling and computational docking studies.