

# TARGETING *CRYPTOSPORIDIUM* GST FOR RATIONAL DRUG DISCOVERY AGAINST PARASITIC INFECTIOUS DISEASES

T Khoza<sup>1</sup>, S M Mfeka<sup>1</sup> and I Achilonu<sup>2</sup>

<sup>1</sup>University of KwaZulu Natal, South Africa

<sup>2</sup>PSFRU-University of the Witwatersrand, South Africa

Infectious diseases caused by intracellular parasitic organisms continue to cause chronic and debilitating conditions in the poorest most disadvantaged areas worldwide. Gastroenteritis is amongst the parasitic infection disease of concern, and is caused by *Cryptosporidium* sp. Gastroenteritis is usually self-limiting in immunocompetent individuals; however life-threatening complications are generally observed with immune compromised patients particularly those with AIDS. Proteins involved in the redox systems have been shown to be crucial for the survival of the parasite, especially intracellular parasites including *Cryptosporidium*, *Plasmodium* and *Schistosoma*. These parasites, uses redox and the anti-oxidation systems to prevent cellular damage resulting from oxidative stress. Among the array of enzymes involved in the redox pathways is glutathione transferase (GST) and transcriptome profile of the parasite has shown that GST transcription is present at all stages of the parasite's life attesting to the importance of GST in the parasite. Subsequently, targeting GST for rational drug discovery is viewed as promising prospect using rational ligand design that can inhibit *Cryptosporidium* GST (Crypto-GST). The only hindrance to this approach is the absence of detailed structural and functional information on Crypto-GST. To this end, we have cloned and expressed Crypto-GST and currently optimising its crystallisation conditions. Furthermore, our preliminary data using bioinformatics and homology modelling shows that, Crypto-GST has a low sequence similarities between the parasite GSTs and human GST classes, despite the structural conservation across the GST classes. Thus, to selectively inhibit parasite GSTs without effectively inhibiting human GSTs is plausible, if these differences in primary sequence are comprehensively exploited for rational drug design. Structural elucidation of Crypto-GST using crystallography will enable to successfully employ rational drug design and discovery targeting Crypto-GST, thus addressing the health burden associated *Cryptosporidium* infection especially in immune compromised patients particularly those with AIDS.

KhozaT1@ukzn.ac.za