Title: Population genomics of praziquantel treatment response by *Schistosoma mansoni* from Uganda

Human populations at risk of schistosomiasis, particularly in sub-Saharan Africa, typically receive treatment with Praziquantel (PZQ) via annual mass drug administration programmes to reduce morbidity and to control transmission. These programmes have successfully decreased the prevalence and intensity of infections in many endemic countries; however, the impact of the drug pressure on the *Schistosoma (S.)* populations, particularly at the genetic level, is poorly understood and understudied. This project aims to characterise the genomic diversity of Ugandan *Schistosoma mansoni* populations (pre- and post-PZQ treatment) to determine the impact of PZQ treatment from a clinical trial that aimed to find the appropriate treatment regimen for preschool-aged children with intestinal schistosomiasis in Lake Albert, Uganda. Eggs were collected from participant stool, hatched, and individually stored on QIAcard FTA cards. Low-input DNA recovery followed by library preparation and multiplexing was undertaken before whole genome sequencing of 96 individual miracidia sequencing libraries using 150 bp paired-end reads on an Illumina Novaseq S4 lane. Mean coverage was calculated in 25kb sliding windows and ranged from 0.1x-16.5x coverage of the *S. mansoni* genome (version 10). We characterised the population structure and genomic diversity of *S. mansoni* populations within the context of published genomic data from different regions of Uganda and five other countries. Principal component analysis revealed that parasites from Lake Albert form a panmictic population and show a lack of population structuring. However, clear population structuring was shown at the regional and country level where parasites from Lake Albert could be distinguished from Lake Victoria and Koome Islands. We detected no high-frequency functionally impactful variants in the candidate PZQ target, the transient receptor potential melastatin praziquantel channel ($SmTRPM_{PZQ}$). In conclusion, our findings suggest that PZQ treatment has not had a significant impact on the population structuring of parasites in Lake Albert. As control efforts to eliminate schistosomiasis intensify to reach the WHO neglected tropical disease roadmap targets, there is a need to monitor how *Schistosoma* populations are evolving in response to treatment. The lack of high frequency functionally impactful variants in $SmTRPM_{PZQ}$ found makes PZQ resistance difficult to monitor currently.