GENOMIC SURVEILLANCE OF *SCHISTOSOMA HAEMATOBIUM* IN ZANZIBAR TO MONITOR PRAZIQUANTEL EFFICACY AS PART OF THE RESISTANCE EVALUATION AND SURVEILLANCE INITIATIVE FOR SCHISTOSOMIASIS TREATMENT (RESIST)

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Background and Aims

Despite >25 years of praziquantel (PZQ) mass drug administration targeting *Schistosoma haematobium* (*Sh*) in Pemba (Zanzibar), transmission persists, with local prevalences up to 35% reported in 2025, raising concern for PZQ efficacy. Using a genomic surveillance approach, this project aims to identify genetic determinants associated with reduced PZQ responsiveness within *Sh* populations exposed to long-term treatment pressure.

Methods

Representing *Sh* populations subjected to intensive PZQ treatment, whole-genome sequencing was performed on 300 individual miracidia from 172 children attending 17 Pemba schools in 2012 and 2017. Analyses focused on the recently identified PZQ molecular target, $\mathrm{TRPM_{PZQ}}$, with variants characterised relative to *S. mansoni* orthologues previously described, and using a cytoplasmic $\mathrm{Ca^{2+}}$ reporter assay measuring $\mathrm{TRPM_{PZQ}}$ activity relative to the *Sh* wild-type in lab generated mutants. In addition, miracidia were collected in 2024–2025 from children attending the same 17 schools as part of a large-scale surveillance programme.

Results

Analysis of 2012/2017 samples identified 211 (3.1%) variant sites within $\mathrm{TRPM_{PZQ}}$. Three mutations detected at low allele frequencies (AF<0.01) were profiled as having reduced PZQ responsiveness, whilst four others caused no difference in PZQ sensitivity. In

2024/2025, 12,598 miracidia were collected from 428 children, including 14 individuals who were positive post-PZQ treatment.

Conclusions

This is the first large-scale spatiotemporal genomic surveillance of *Sh* in relation to PZQ treatment. Allele frequency shifts of TRPM_{PZQ} variants attributed with decreased PZQ sensitivity in 2012/2017 *Sh* populations will be monitored in 2025-2025. Analysis of 2024–2025 samples will enable assessment of PZQ-mediated selection and inform control and elimination strategies.