Gene expression profiling of polyamine depleted malaria parasites using SSH and DNA microarray

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Sub-Saharan Africa suffers extensively from the burden of the malaria with almost all deaths and severe disease caused by *Plasmodium falciparum*. Increasing resistance of the parasite to most known anti-malarials serves to compound this problem. Protein structure-based design is an ideal strategy for the development of novel anti-malarial drugs, although the limiting factor in this drug discovery process is the identification of key protein targets in the parasite. One particularly interesting target is polyamine metabolism as the parasites are essentially totally dependent on polycations for normal division and differentiation. Currently, comprehensive information is not available on the exact function of the polyamines in *P.falciparum*. This study aims to identify additional potential targets in polyamine metabolism for use in drug discovery by applying transcriptional profiling.

We investigated the effect of polyamine depletion on the transcriptome of malaria parasites. Suppression, subtractive hybridisation (SSH) was used to generate libraries containing approximately 900 clones each of genes that were respectively up- or down-regulated in the absence of polyamines. These were subsequently screened using DNA microarray as a semi high-throughput screening method. The advantage of this approach is the use of a preselected library (ie an 'open system'), where one can evaluate the expression pattern of thousands of genes. Targets used for hybridization against these libraries consisted of samples taken from treated and untreated parasites at several time points spanning the 48-hour erythrocytic schizogony cycle of the parasite. Results are analysed and processed by in-house developed data processing and analysis pipelines, to obtain a metabolic profile of parasites depleted of polyamines. Furthermore, interacting partners/pathways and the exact mode-of-action of a polyamine biosynthesis inhibitor will be deduced.

Project funded by NRF Innovation Fund 'Novel Drug Development Platform' TM1002FP.