



## Real time imaging of the glutathione redox potential and import of host peroxiredoxin 2 in the malarial parasite *Plasmodium falciparum*

By Denis Kasozi Matovu

Shaker Verlag Jun 2012, 2012. Buch. Condition: Neu. Neuware - Malaria caused by the most lethal *Plasmodium* species, *P. falciparum*, remains a major global health problem to almost half the world's population. To contribute to the identification of novel drug targets and the development of rationally effective combination therapies three approaches to support novel drug discovery strategies were explored in this thesis. First, the role of the glutathione redox potential (EGSH) in the mechanism of drug action and resistance in malaria parasites was systematically studied. Using a EGSH biosensor, comprising human glutaredoxin-1 linked to a redox sensitive green fluorescent protein (hGrx1-roGFP2), the basal cytosolic EGSH as well as the antimalarial drug-induced changes in EGSH were determined in drug-sensitive (3D7) and resistant (Dd2) strains of *P. falciparum*. By confocal microscopy, the ability of hGrx1-roGFP2 to rapidly react to changes in EGSH due to oxidative and nitrosative stress was demonstrated. Importantly, the cytosolic basal EGSH of 3D7 and Dd2 strains was found to be  $-314.2 \pm 3.1$  mV and  $-313.9 \pm 3.4$  mV, respectively, which is suggestive of a highly reducing cytosol. Among the tested antimalarial drugs, only methylene blue (MB) rapidly, on scale of minutes, oxidized glutathione (GSH). Notably, following 24...



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