

***PLASMODIUM FALCIPARUM* HISTIDINE-RICH PROTEIN II AS AN INDICATOR OF PARASITE GROWTH AND DEVELOPMENT OF A NEW MALARIA DRUG SUSCEPTIBILITY ASSAY**

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Although *Plasmodium falciparum* Histidine-Rich Protein II (PfHRP2) has been known for more than a decade, its application remained limited to the diagnosis of *falciparum* malaria. Due to its widespread use in malaria rapid diagnostic devices, it is currently one of the best documented malaria proteins. However, little is known about the development of HRP2 concentrations under the influence of antimalarial drugs. To evaluate the potential of HRP2 for use in drug sensitivity and bioassays, the HRP2 levels in cell medium mixture, cellular compartment, and in culture supernatant were determined by a double-site sandwich ELISA in a number of culture adapted strains of *P. falciparum*. Characteristic increases in the overall HRP2 levels were found during the later ring and the trophozoite stages, when the maximum increase in parasite cytoplasm was seen. During the later schizont development, rupture, and reinvasion, however, the HRP2 levels remained relatively stable. Generally the development of HRP2 concentrations corresponded very well to the increase in parasitemia when followed over a full life cycle. When antimalarial drugs were added to the culture at levels that inhibited parasite growth, the production of HRP2 was inhibited to the same extent. After the addition of high drug concentrations the overall HRP2 levels remained constant, the distribution within the cell medium mixture, however, changed in favor of the supernatant due to the considerably higher concentration in the cellular compartment and constant release into the medium. When the cultures were exposed to serial dilutions of antimalarial drugs a distinct inhibition of HRP2 production was seen with increasing amounts of drugs, which resulted in a sigmoid dose-response curve and reflected parasite growth inhibition as assessed by microscopy. HRP2, therefore allows for an accurate estimation of parasite growth and its inhibition and is well suited for use in drug sensitivity tests or bioassays. Based on this knowledge a novel drug sensitivity assay for *P. falciparum* was developed, which is very sensitive, straightforward and simple to establish and perform. It offers a number of advantages over traditional assays while providing results that are highly comparable to those of conventional tests.

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