PhD defence Harvie Portugaliza (online)

Targeting Malaria Transmission: A Transdisciplinary Approach

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Dit is de omschrijving

Link

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Summary

To achieve malaria elimination, great emphasis must be put on targeting the parasite's transmissible stages, so that, along with effective treatment of clinical malaria caused by asexual stages, complete interruption of the life cycle can be achieved. Unfortunately, the sustainable goal of interrupting malaria transmission is more complex than previously thought, as demonstrated by the many failed attempts to eradicate the parasite. One of the various reasons why interrupting malaria transmission is challenging is that the transmissible gametocytes are resilient and complex in nature. The adaptable nature of the malaria parasite suggests that enhanced gametocyte production is a response to adverse environments. Although gametocytes are constitutively formed at a very low frequency, mounting evidence supports that external factors modulate the rate of sexual conversion by increasing or decreasing gametocyte production. However, whether the most effective antimalarial drug artemisinin can stimulate sexual conversion, which would result in increased production of functional gametocytes in *P. falciparum*, remains to be clarified both under laboratory culture conditions and in field settings. We addressed this research question by first creating a robust assay that measures the sexual conversion rate (**Chapter 2**), and finally tested the impact of artemisinin on sexual conversion and the transmissibility of artemisinin-induced gametocytes to mosquitoes (**Chapter 3**). We extended the scope of our study beyond the laboratory format by looking into how treatment affects the sexual conversion of parasites from naturally-infected patients. We speculate that the current form of malaria treatment, which is artemisinin-based combination therapy (ACT) and artesunate monotherapy followed by ACT, may stimulate the expression of the sexual commitment gene *pfap2-g* and other sexual ring biomarkers. Hence, this would result in a subsequent increase in the production of circulating mature gametocytes (**Chapter 4**). Our *in vitro* study permitted a detailed dissection of the effect of artemisinin exposure on parasite sexual conversion, while our field studies probed how translatable our *in vitro* results are to real human malaria infections, which are naturally complex due to interaction of multiple factors (e.g., immunity and LysoPC levels) inside the human body. Our study designs are therefore complementary to address the impact of artemisinin on parasite's investment on transmission. Lastly, we believe that by understanding the community perceptions of malaria, including its malaria-related interventions, we will be able to tailor the right approach for site-specific malaria elimination campaigns. In this way, we may gain new insights on how a new tool, such as mass drug administration (MDA), can be potentially harnessed to completely interrupt malaria transmission (**Chapter 5**).