PhD defence of Hong Van Nguyen

Contribution of molecular tools to malaria elimination in Vietnam

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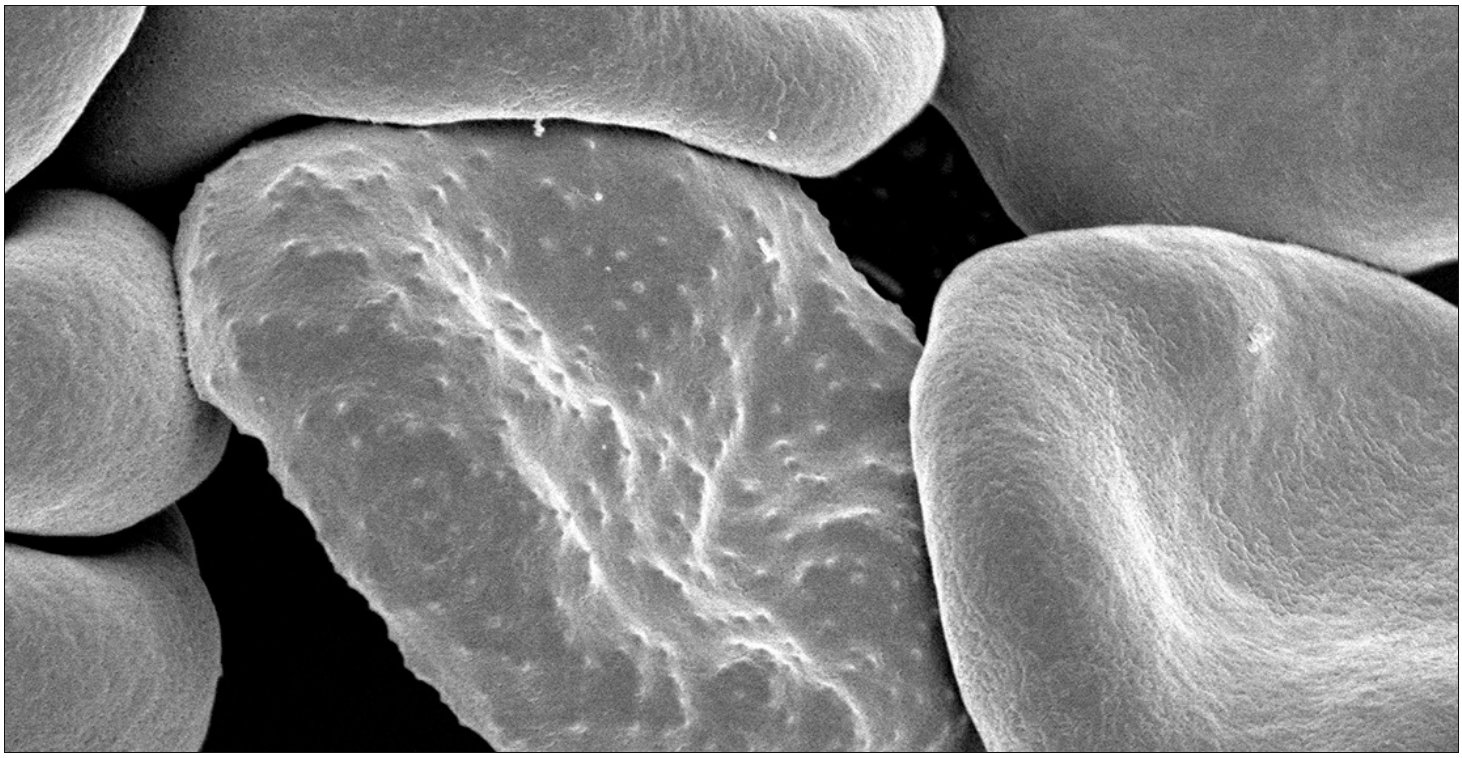

Dit is de omschrijving

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Summary:

This thesis aims to advance the development and application of molecular tools to better our understanding of malaria epidemiology and transmission in Vietnam, and improve surveillance and knowledge of antimalarial drug resistance in the country.

A modified semi-nested multiplex malaria PCR (SnM-PCR) assay was developed and validated to identify all five Plasmodium species infecting humans (including *P.knowlesi)* that are present in Vietnam. SnM-PCR was used to investigate the human malaria reservoir in Ninh Thuan province. While the prevalence of infection was two-fold higher by PCR than light microscopy, we detected a high proportion of asymptomatic infections (81.5%) occurring in all age groups, and a remarkable proportion of mixed infections (25%), demonstrating a large human reservoir in forested areas of the central region.

In addition, we evaluated the genetic complexity of *P.vivax* populations in 4 rural communities in central Vietnam. Population genetic analysis using 14 polymorphic loci showed moderate genetic diversity (*He*= 0.68) and a high proportion of polyclonal infection (71.3%), despite linkage disequilibrium (LD) was detected in the whole population and in each community, suggesting gene flow within and among communities. 101 haplotypes were found, of which 84 were defined as unique. Related haplotypes was quite common in these four communities, with low genetic differentiation being observed.

Next, we investigated *P.falciparum* development of artemisinin resistance in Quang Nam by following 89 *P. falciparum* infected patients in a 42-day *in vivo* and *in vitro* efficacy study. Despite a high Adequate Clinical and Parasitological Response (APCR: 97.7%), the day three (D3) positivity reached 29.2%, which is indicative of resistance. The I534T-K13 mutation was the most frequent (80.7%) and on D0 its presence was associated with delayed parasite clearance (PCT≥72h).

Finally, we reported a case of a Vietnamese worker that after 3 years in Angola returned to Vietnam with a *P. falciparum* singe infection confirmed by species-specific PCR. He did not respond to intravenous artesunate and clindamycin treatment, nor to an oral artemisinin-based combination. This case provides evidences of early treatment failure of *P. falciparum* with ACT, prompting effors to predict, detect, and mitigate the threat of antimalarial drug resistance in Africa.

In conclusion, in areas of low transmission such as Vietnam, implementation of molecular methods in control and elimination programs increases efficiency of surveillance strategies.