



# Unraveling the Enigma: Tackling Knowlesi Malaria in Southeast Asia

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### Editorial

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**Abbreviations:** PCR: Polymerase Chain Reaction; RON: Rhoptry Neck Protein; NHPs: Nonhuman Primates; SICAvAr: Schizont-Infected Cell Agglutination Variant; KIR: Knowlesi Interspersed Repeat.

### Editorial

*Plasmodium knowlesi*, a malaria parasite found predominantly in Southeast Asia, presents a significant

challenge to public health due to its ability to infect both humans and non-human primates (NHPs). Mosquito vectors of *Plasmodium knowlesi* are primarily *Anopheles hackeri* and *Anopheles latens*. Recent advancements in molecular detection have led to a surge in reported cases of knowlesi malaria, shedding light on its prevalence. However, it's becoming increasingly evident that environmental factors, such as deforestation, play a critical role in facilitating the spread of this disease. To effectively address the threat of knowlesi malaria, it's imperative to comprehend the intricate interactions among humans, NHPs, mosquitoes, and the environment (Figure 1).

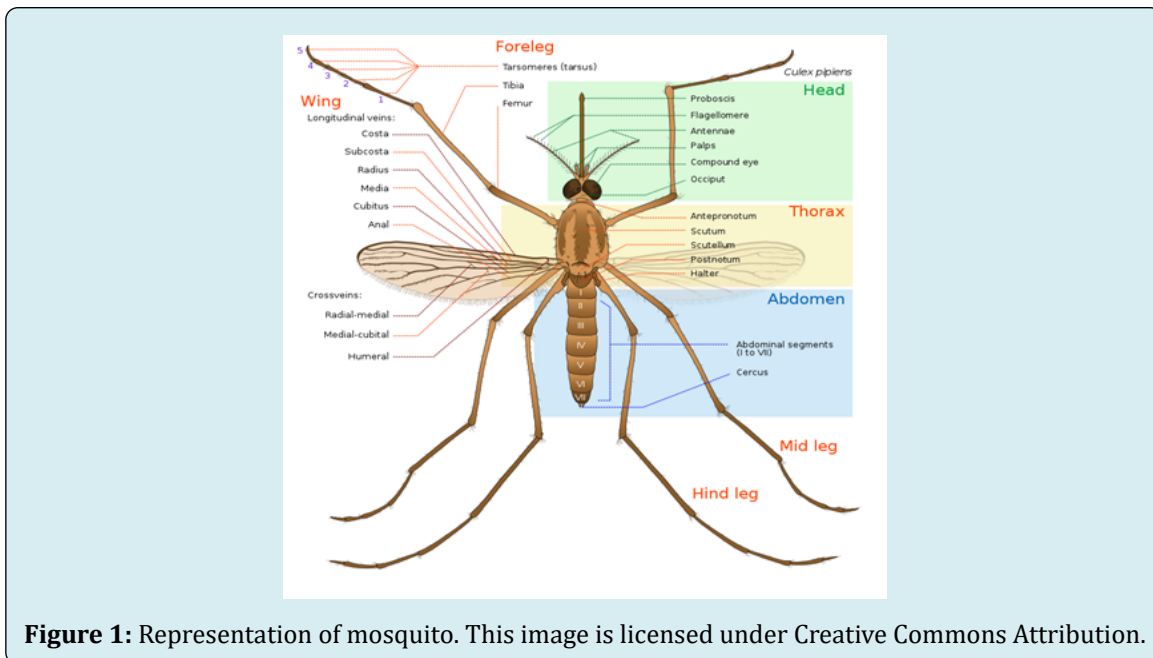


Figure 1: Representation of mosquito. This image is licensed under Creative Commons Attribution.

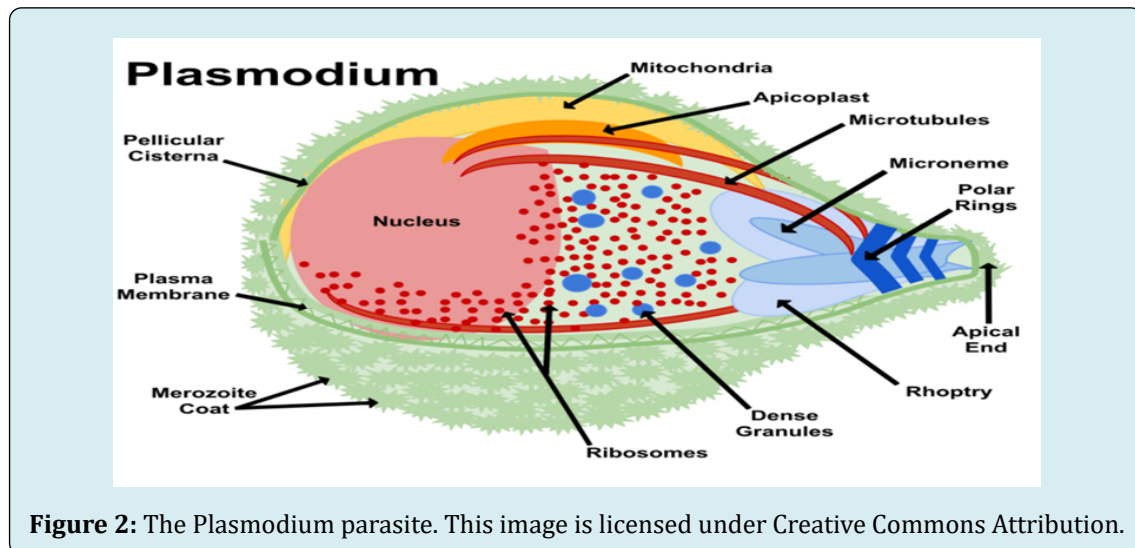
The genome of *Plasmodium knowlesi*, spanning 23.5 megabases across 14 chromosomes, harbors unique genes

like SICAvAr and Kir, pivotal in the parasite's biology and its interaction with hosts. Deciphering the roles and regulation



of these genes holds paramount importance for devising effective malaria control and treatment strategies [1]. *Plasmodium knowlesi*, a malaria-causing parasite, employs specialized structures at its apical end to invade host cells, including rhoptries, micronemes, and dense granules that release effector molecules. Rhoptries release proteins like

RON crucial for invasion, forming the moving junction. The malaria parasite possesses mitochondria and an apicoplast inherited from endosymbiosis, with the apicoplast housing essential metabolic pathways essential for survival and proliferation despite lacking photosynthetic function [2,3] (Figure 2).



*Plasmodium knowlesi*, a type of malaria parasite, closely resembles *Plasmodium vivax* but originates from macaques. Macaques are its main hosts, highlighting the interaction between primates and infectious diseases and the dynamics of zoonotic transmission within ecosystems [4]. Nonhuman primate (NHP) malaria, including parasites like *Plasmodium knowlesi*, presents a significant challenge to malaria control efforts. Other zoonotic parasites such as *Plasmodium*

*cynomolgi*, *Plasmodium simian*, and *Plasmodium inui* further complicate the situation. However, molecular techniques like polymerase chain reaction and gene sequencing have helped identify and comprehend the importance of *Plasmodium knowlesi* in human malaria cases. This understanding is crucial for devising effective strategies against malaria, especially in areas with prevalent zoonotic malaria parasites [5] (Figure 3).



Deforestation in Southeast Asia is associated with a rise in knowlesi malaria cases. Clearing forests for agriculture brings humans closer to macaque hosts and mosquito vectors, increasing the risk of parasite transmission through mosquito bites. Addressing knowlesi malaria demands a comprehensive strategy considering human and ecological elements. It includes enhancing surveillance and detection

methods alongside initiatives to counteract environmental changes like deforestation. Researchers and public health officials can devise effective prevention and control strategies in Southeast Asia by comprehending the intricate interplay among humans, primates, mosquitoes, and the environment [6] (Figure 4).



**Figure 4:** The Map of Southeast Asia. This image is licensed under Creative Commons Attribution.

Knowlesi malaria, a zoonotic disease, is influenced by human activities and the adaptability of parasites and vectors. Effective strategies are crucial for prevention, diagnosis, and treatment. Rapid diagnostic tests are essential to promptly address *Plasmodium knowlesi* infections, mitigating complications, mortality, and drug resistance [7-27].

*Plasmodium knowlesi* presents a challenge in malaria control efforts, given its zoonotic nature and close resemblance to *Plasmodium vivax*. Research involving NHPs has significantly advanced our understanding of malaria, highlighting the importance of studying zoonotic parasites like *Plasmodium knowlesi*. Addressing knowlesi malaria requires an approach that encompasses the mitigation of environmental changes such as deforestation.

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