



RECOMMENDATION

Malaria host manipulation increases probability of mosquitoes feeding on humans

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Based on reviews by:
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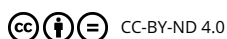
A recommendation of

Vantaux A, Yao F, Hien DF, Guissou E, Yameogo BK, Gouagna LC, Fontenille D, Renaud F, Simard F, Constantini C, Thomas F, Mouline K, Roche B, Cohuet A, Dabire KR, and Lefevre T. Field evidence for manipulation of mosquito host selection by the human malaria parasite, *Plasmodium falciparum*. *bioRxiv*, 207183 ver. 6 peer-reviewed and recommended by *PCI Evol Biol* (2018). DOI: 10.1101/207183

Parasites can manipulate their host's behaviour to ensure their own transmission. These manipulated behaviours may be outside the range of ordinary host activities [5], or alter the crucial timing and/or location of a host's regular activity. Vantaux *et al.* show that the latter is true for the human malaria parasite, *Plasmodium falciparum* [6]. They demonstrate that three species of Anopheles mosquito were 24% more likely to choose human hosts, rather than other vertebrates, for their blood feed when they harboured transmissible stages (sporozoites) compared to when they were uninfected, or infected with non-transmissible malaria parasites [6]. Host choice is crucial for the malaria parasite *Plasmodium falciparum* to complete its life-cycle, as their host range is much narrower than the mosquito's for feeding; *P. falciparum* can only develop in hominids, or closely related apes [4].

The study only shows this stage-dependent parasite manipulation retrospectively (by identifying host type and parasite stage in mosquitoes after their blood feed [6]). There was no difference in the preferences of infectious (with sporozoites) or un-infectious (infected without sporozoites, or uninfected) mosquitoes between human versus cow hosts in a choice test [6]. This suggests that the final decision about whether to feed occurs when the mosquito is in close range of the host.

This, coupled with previous findings, shows that vector manipulation is a fine-tuned business, that can act at multiple stages of the parasite life-cycle and on many behaviours [2]. Indeed,



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mosquitoes with non-transmissible *Plasmodium* stages (oocysts) are more reluctant to feed than sporozoite-infected mosquitoes [1] as vectors can be killed by their host whilst feeding, doing so before they are ready to transmit is risky for the malaria parasite. Thus, it seems that *Plasmodium* is, to some extent, master of its vector; commanding it not to feed when it cannot be transmitted, to feed when it is ready to be transmitted and to feed on the right type of host. What does this mean for our understanding of malaria transmission and epidemics?

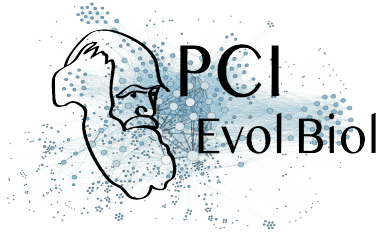
Vantaux *et al.* use a mathematical model, parameterised using data from this experiment, to highlight the consequences of this 24% increase in feeding on humans for *P. falciparum* transmission. They show that this increase raises the number of infectious bites humans receive from 4 (if sporozoite-infected mosquitoes had the same probability as uninfected mosquitoes) to 14 (an increase in 250%), for mosquitoes with a 15-day life-span, at ratios of 1:1 mosquitoes to humans. Longer mosquito life-spans and higher ratios of mosquitoes to humans further increases the number of infectious bites.

These results [6] have important implications for epidemiological forecasting and disease management. Public health strategies could focus on possible ways to trap sporozoite-infected mosquitoes, mimicking cues they use to locate their human hosts, or identify the behaviour of mosquitoes harbouring non-yet infectious *Plasmodium*, and trap them before they bite. Moreover, the results of the model show that failing to take into account the preference for humans of sporozoite-infected mosquitoes could underestimate the size of pending epidemics.

An important question previously raised is whether *Plasmodium*-induced alteration in host behaviour really is manipulation, or just a side-effect of being infected [1, 2]. The fact that Vantaux *et al.* show that these altered feeding behaviours increases the likelihood of transmission, in that a sporozoite-infected mosquito is more likely to feed on a human, strongly suggests that it is adaptive for the parasite [6]. Ultimately, to show that it is manipulation would require the identification of molecular factors released by *Plasmodium* that are responsible for physiological changes in the mosquito [3].

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Appendix

Reviews by Ricardo S. Ramiro, Olivier Restif and an anonymous reviewer, DOI: 10.24072/pci.evolbiol.100057