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The Evolutionary Origin of *Plasmodium falciparum*

Among species of *Plasmodium*, *P. falciparum* is an enigma. It is unusually pathogenic and is not characterized by the relapsing episodes characteristic of other species. Its primary vector is a species of mosquito that is highly anthropophilic (*Anopheles gambiae*), and which shows evidence of rapid genetic change apparently coincident with the rise of human agriculture. *Plasmodium falciparum* has no alternative vertebrate reservoir hosts, and if the number of human infections drops below a threshold level, the species is unable to maintain itself. All of these observations suggested a novel hypothesis to Boyd (1949, cited in Waters et al. [1991]), who proposed that *P. falciparum* is a relatively new species that originated when the advent of agriculture brought humans and certain types of mosquitoes into contact on a regular basis.

Building upon Boyd's hypothesis, Waters et al. (1991) investigated the evolutionary origins of *P. falciparum* in more detail. They utilized fragments of asexually expressed small-subunit ribosomal RNA converted to estimates of genetic distances to generate phylogenetic trees for several species of *Plasmodium* infecting rodents, primates (including humans), and birds. They concluded that Boyd's hypothesis about the recent origin of *P. falciparum* was upheld by the position of that parasite on the phylogenetic tree. They further postulated that *P. falciparum* originated via a host switch from birds to humans because it formed a monophyletic group with the 2 species of avian *Plasmodium* examined. This would require 1 of 2 events: either a species of mosquito that was regularly a vector for some avian-inhabiting *Plasmodium* species began feeding on humans because it formed a monophyletic group with the 2 species of avian *Plasmodium* examined. This would require 1 of 2 events: either a species of mosquito that was regularly a vector for some avian-inhabiting *Plasmodium* species began feeding on humans as well, or a species of mosquito that regularly fed on humans began feeding on birds as well. The high degree of pathogenicity and unusual biology of *P. falciparum* is thus explained by its being a relatively young species and by its origin via a host switch, both because it formed a monophyletic group with avian *Plasmodium* species and because it is one of the few that feed on humans. The high degree of pathogenicity and unusual biology of *P. falciparum* is thus explained by its being a relatively young species and by its origin via a host switch, both because it formed a monophyletic group with avian *Plasmodium* species and because it is one of the few that feed on humans.

Monophyly by itself, however, does not tell us whether the ancestor of *P. falciparum* switched from primates to birds or from birds to primates (Fig. 1). To choose between these 2 alternatives, it is necessary to examine the host relationships of other members of *Plasmodium* and use phylogenetic optimization procedures to infer the direction of host switching. Fortunately, these data were provided by Waters et al. (1991). Phylogenetic optimization (see Brooks and McLennan [1991] and Wiley et al. [1991] and references therein) of host types onto their 2 trees unambiguously supports the conclusion that *Plasmodium* species infecting birds are derived from a group of *Plasmodium* species inhabiting primates, specifically human primates (Fig. 2).

Waters et al. (1991) addressed 2 questions. First, from where did *P. falciparum* come? According to the host data and phylogenetic relationships presented in their paper, the ancestor of *P. falciparum* is the sister species of *Plasmodium malariae*. Its antecedents are thus strictly "human"; i.e., the parasite speciated in association with the ancestral host type. Second, why is *P. falciparum* so virulent? The phylogenetic trees presented by Waters et al. (1991) are consistent with Boyd's hypothesis that *P. falciparum* is the most recently derived species of *Plasmodium* inhabiting humans. Although the trees do not support their hypothesis that the evolutionary origin of *P. falciparum* is associated with a host switch, this does not preclude a role for the appearance of agriculturally based communities on the parasite's subsequent evolutionary trajectory. The origin of *P. falciparum* may be explained by an interaction between its recent age and changes in human evolution that created conditions under which a highly pathogenic species of *Plasmodium* could evolve and be maintained. This scenario supports Anderson and May's (1982) contention that "the coevolutionary trajectory followed by any particular host–parasite association will ultimately depend on the way the virulence and the production of transmission stages of the parasite are linked together: depending on the specifics of this linkage, the coevolutionary course can be towards essentially zero virulence, or to very high vir-
ulence, or to some intermediate grade." These results also indicate that the rise of human agriculture played a role in the evolution of avian malarias. Some avian malarias may have arisen by host switching from humans when agricultural practices brought humans and birds into close contact on a regular basis. If this hypothesis is supported by analysis of further data, then it means that many of the extant avian malarias have evolved over a very short period of time.

The trees produced by Waters et al. (1991) represent a preliminary attempt to address the question of the evolutionary origin of *P. falciparum*. As they noted in their conclusion, a larger number of *Plasmodium* species needs to be analyzed to provide a more robust...
Phylogenetic framework from which to draw conclusions about host and parasite evolutionary patterns. It is possible that the addition of more species will alter the phylogenetic relationships and ultimately provide support for their host switching hypothesis. There are 2 types of phylogenetic patterns that would support the hypothesis that *P. falciparum* is derived from avian *Plasmodium* spp. In the first case (Fig. 3), the avian *Plasmodium* species and the primate *Plasmodium* species, excluding *P. falciparum*, are monophyletic groups (in Fig. 2 the primate-inhabiting *Plasmodium* species form a paraphyletic group). This would unambiguously support their hypothesis, emphasizing that *P. falciparum* is only distantly related to the other *Plasmodium* species inhabiting humans. In the second case (Fig. 4), we would explain the origin of *P. falciparum* as the result of a transfer from birds to humans, but the origin of the avian malarias would still involve an earlier host switch from other primate malarias. In this scenario, birds would be said to have acquired *Plasmodium* from humans, followed by a reverse host switch, resulting in *P. falciparum*. Overall, in order for the Waters et al. (1991) host-switching hypothesis to be supported, *P. falciparum* must be nested within the avian-inhabiting *Plasmodium* species regardless of the phylogenetic relationships among other *Plasmodium* species.

In any event, it would appear that a larger number of *Plasmodium* species needs to be analyzed, and that phylogenetic trees based upon a variety of different data sets need to be generated. This would provide a more powerful phylogenetic framework from which to draw conclusions about host and parasite evolutionary patterns. Comparisons of the new phylogenetic trees with the variety of patterns predicted from various coevolutionary and host-switching phenomena presented herein (and in Ronquist and Nylin [1990] and Brooks and McLennan [1991]) would then provide the most robust explanations about the evolutionary origins of *P. falciparum*. At present, *P. falciparum* remains an enigma.

**LITERATURE CITED**


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