Title
Reply to Sharp et al.: Host species sampling bias and Plasmodium falciparum origin paradigm shifts

Journal
Proceedings of the National Academy of Sciences of the United States of America, 108(43)

ISSN
0027-8424

Authors
Prugnolle, Franck
Durand, Patrick
Ollomo, Benjamin
et al.

Publication Date
2011-10-25

DOI
10.1073/pnas.1112821108

LETTER

Reply to Sharp et al.: Host species sampling bias and *Plasmodium falciparum* origin paradigm shifts

We thank Sharp et al. (1) for their comments, but we disagree. The results of Prugnolle et al. (2) did not disprove that human *Plasmodium falciparum* has a gorilla origin but brought that conclusion into question, which is what we asserted (and yes, a single isolate in a single monkey species is enough to question it).

Current data can be accounted for by the hypothesis of a gorilla origin of human *P. falciparum*, but there are alternatives (reviewed in ref. 3). These alternative hypotheses need to be considered and tested. The available data could be biased or incomplete. Liu et al.'s sample [reference 2 in the Sharp et al. letter (1)] was large, but it concerned only three great ape species. It remains to be explored whether *P. falciparum*-related strains circulate in other primate species. Samples that include only great apes may not yield the complete picture.

Consider how hypotheses concerning the origin of *P. falciparum* have changed. Up to 1994, only avian and rodent, in addition to human, *Plasmodium* isolates had been genetically characterized. The hypothesis favored was that *P. falciparum* originated from a transfer from birds or rodents. In 1994, *Plasmodium reichenowi*, isolated from a chimpanzee, was characterized. The new evidence favored the hypothesis that *P. falciparum* and *P. reichenowi* diverged in association with the divergence of their respective hosts, humans and chimpanzees. In 2009, analysis of *Plasmodium* isolates circulating in chimpanzees in Africa demonstrated that the diversity of the *Plasmodium* lineages circulating in this host species was larger than previously reported (4). The results favored the hypothesis that human *P. falciparum* resulted from a horizontal transfer of parasites from chimpanzees to humans. In 2010, new isolates from bonobos favored the hypothesis that human *P. falciparum* originated from a horizontal transfer from bonobos (5). However, in the same year, *P. falciparum* isolates discovered in wild gorillas indicated that transfers may occur between humans and gorillas, although the small size of the genetic samples did not allow conclusions to be drawn regarding the direction of the transfers (6). Analysis of many additional isolates from gorillas and larger genetic sequences, however, favored the hypothesis that human *P. falciparum* originated from a single cross-species transfer from gorillas [reference 2 in the Sharp et al. letter (1)].

This brief history shows that the study of new host species (and thus new *Plasmodium* isolates) has repeatedly favored changes in the paradigm regarding the origin of *P. falciparum*. There is a need for additional investigations to ascertain whether *P. falciparum*-related strains are present in other primate species. The parasite observed in a monkey (2) may or may not have originated by a transfer from gorilla to monkey, but it remains to be ascertained how frequently related transfers occur in nature and whether they will favor the origin of human *falciparum* from gorillas or from other primates. Indeed, the discovery of a new primate species infected by a related primate-specific strain of *P. falciparum* (2) questions the gorilla origin hypothesis.

***Franck Prugnolle*[a,1], *Patrick Durand*[a], *Benjamin Ollomo*[b], *Francisco J. Ayala*[c,1], *and François Renaud*[a,1]**

[a]*Laboratoire Maladies Infectieuses et Vecteurs Écologie, Génétique, Évolution et Controle, Unité Mixte de Recherche 224, Centre National de la Recherche Scientifique-Institut de Recherche pour le Développement-UM1, Institut de Recherche pour le Développement Montpellier, BP 64501, 34394 Montpellier Cedex 5, France;* [b]*Unité de Parasitologie Médicale, Centre International de Recherches Médicales de Franceville, BP 769, Franceville, Gabon; and* [c]*Department of Ecology and Evolutionary Biology, University of California, Irvine, CA 92697-2525*

1. Sharp PM, et al. (2011) Source of the human malaria parasite *Plasmodium falciparum*. *Proc Natl Acad Sci USA* 108:E744–E745.
2. Prugnolle F, et al. (2011) African monkeys are infected by *Plasmodium falciparum* nonhuman primate-specific strains. *Proc Natl Acad Sci USA* 108:11948–11953.
3. Prugnolle F, et al. (2011) A fresh look at the origin of *Plasmodium falciparum*, the most malignant malaria agent. *PLoS Pathog* 7:e1001283.
4. Rich SM, et al. (2009) The origin of malignant malaria. *Proc Natl Acad Sci USA* 106: 14902–14907.
5. Krief S, et al. (2010) On the diversity of malaria parasites in African apes and the origin of *Plasmodium falciparum* from Bonobos. *PLoS Pathog* 6:e1000765.
6. Prugnolle F, et al. (2010) African great apes are natural hosts of multiple related malaria species, including *Plasmodium falciparum*. *Proc Natl Acad Sci USA* 107: 1458–1463.

Author contributions: F.P., P.D., B.O., F.J.A., and F.R. wrote the paper.

The authors declare no conflict of interest.

[1]To whom correspondence may be addressed. E-mail: fjayala@uci.edu, franck.prugnolle@ird.fr, or francois.renaud@ird.fr.