erved in all but 1 (SVMDT) of the 7 haplotypes identified among the 147 clones from a subset of East Sepik Province samples collected in 2001–2003 [6]. The complete replacement of 76K by 76T was indicative of potent CQ selective pressure.

We estimated diversity by comparing the frequencies of minor pfcrt sequence variants between the 2 sampling periods and found no statistically significant difference (P = .46, t test); thus, parasites from these 2 samples were equally diverse. Our data lend support to the assertion made by Mehlotra et al. [1] that the reduced diversity in microsatellites flanking pfcrt in parasites from the 1980s was most likely a result of a CQ selective sweep (figure 1). The utility of archived samples for retrospective analysis was demonstrated by both Mehlotra et al. [1] and our work [2] and can probably be extended to studies of resistance to other chemotherapeutic agents.

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Reply to Chan et al.

To the Editor—Chloroquine-resistant falciparum malaria in Southeast Asia was first detected at the Cambodia-Thailand border during the late 1950s [1] and supposedly spread steadily in the 1960s–1970s throughout Asia and the Pacific. Chloroquine resistance (CQR) was first reported from West Irian (Irian Jaya, Indonesia) in 1974 [2] and soon after from western and eastern Papua New Guinea (PNG) [3–5]. With the availability of Plasmodium falciparum culture techniques, an early (1979–1983) survey involving >300 children from 78 schools in 12 PNG provinces reported 73% in vitro and 54% in vivo CQR [6], suggesting a rapid spread. The prevalence of CQR-associated parasite gene polymorphisms in the PNG samples collected after 1995 has been documented (pfcrt SVMNT, 40%–83%; pfmdr1 86Y, 47%–88%) [7]. Our recent study [8] suggested that a selective sweep involving the pfcrt locus had occurred before the early 1980s and that the chloroquine-resistant P. falciparum parasites continue to diverge. However, our samples did not enable an evaluation of parasites collected at time points before or during emergence/initial spread of CQR in PNG. To understand the origin, evolution, and spread of CQR from a molecular perspective, it is important to determine the status of parasite gene polymorphisms in samples collected during earlier periods. In this regard, recent observations of Chan et al. on the samples collected before 1970 [9] add interesting and valuable information to this topic.

The observations of Chan et al. [9] show that, before 1974, PNG P. falciparum parasites carried only the chloroquine-sensitive pfcrt allele (CVMNK). Our observations [8], 6–8 years after the initial reports on chloroquine-resistant P. falciparum in PNG, suggested that the pfcrt SVMNT allele was prevalent throughout PNG by the early 1980s. Our observations are consistent with previous in vitro and in vivo identification of chloroquine-resistant P. falciparum strains in PNG soon after the first cases of CQR were reported, suggesting a rapid spread [6]. The report by Chan et al. [9] narrows the period during which parasite genetic polymorphisms associated with CQR first appeared in PNG and further illustrates the value of archival samples for reconstructing the history of the rise and spread of drug resistance in parasites.

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