Monitoring parasite diversity for malaria elimination in sub-Saharan Africa


The African continent continues to bear the greatest burden of malaria and the greatest diversity of parasites, mosquitoes, vectors, and human victims. The evolutionary plasticity of malaria parasites and their vectors is a major obstacle to eliminating the disease. Of current concern is the recently reported emergence of resistance to the front-line drug, artemisinin, in South-East Asia in Plasmodium falciparum, which calls for preemptive surveillance of the African parasite population for genetic markers of emerging drug resistance. Here we describe the Plasmodium Diversity Network Africa (PDNA), which has been established across 11 countries in sub-Saharan Africa to ensure that African scientists are enabled to work together and to play a key role in the global effort for tracking and responding to this public health threat.

Africa is home to the most successful malaria vector (Anopheles gambiae complex) and the deadliest malaria parasite (Plasmodium falciparum). Despite efforts to eradicate malaria in the 1950s and early 1960s, 207 million cases and 627,000 malaria deaths were estimated to have occurred in 2012, mostly in sub-Saharan Africa and in children under 5 years of age (1). The inability to eradicate malaria reflects the complex coevolution of the three eukaryotic genomes involved and represents the major biological challenge to vaccine and drug development. Since publication of the full genome of a reference clone, many other model and population isolates have been sequenced (2), which has provided some insight into the genetic variation responsible for phenotypes like drug resistance and virulence.

However, the global genome-wide pattern of genetic diversity across most endemic regions is poorly understood, as few natural Plasmodium falciparum populations have been analyzed.

Malaria elimination efforts in Africa are heavily reliant on artemisinin combination therapies (ACT) yet no coordinated effort for monitoring emergence or prevention of the spread of artemisinin resistance is in place in Africa. In addition, introduction of new malaria vaccines or mass therapeutic approaches to control and elimination will increase selection for resistance in parasite populations that could damage the effectiveness of these and future tools (Fig. 1).

Rationale and mission for an African Plasmodium Diversity Network

The emergence of antimalarial resistance to artemisinin in Southeast Asia (3, 4) calls for global monitoring of the parasite population (5). The MalariaGEN community has already built a successful framework for data-sharing (6); hence, we have adopted this model to form the Plasmodium Diversity Network Africa (PDNA). The concept of PDNA was seeded by several African scientists during the Genomic Epidemiology of Malaria conference at Hinxton, United Kingdom, in 2012. In May 2013, the network was formally launched in Accra, Ghana, when scientists and clinical researchers met from 13 research groups from across Africa (Fig. 2).

The mission of PDNA is to explore the malaria parasite’s genetic and phenotypic diversity to advance the malaria elimination and eradication agenda in sub-Saharan Africa. We have initiated or will initiate projects to investigate Plasmodium population structure and evolution, to survey the frequencies of current and novel molecular markers of antimalarial drug resistance, and specifically to monitor the emergence and spread of artemisinin resistance in sub-Saharan Africa.

How will PDNA contribute to malaria elimination?

To succeed, malaria elimination requires knowledge of parasite genome variation in different geographical locations and of recent evolutionary selection and a better understanding of the factors that determine gene flow between locations, such as rates of inbreeding and population structure. The PDNA membership represents the range of malaria diversity in Africa. The Network is in its infancy and is bound to evolve with time. Each PDNA member brings specific scientific expertise (table S1) and the capacity to collect local biological material, as well as clinical data. Plasmodium DNA will be either analyzed on site or dispatched

Fig. 1. Queuing for malaria diagnosis in Kisumu County, Kenya. [Photo credit: Hoseah M. Akala, Kenya Medical Research Institute/U.S. Army Medical Research Unit—Kenya]
to various laboratories, such as the Wellcome Trust Sanger Institute, UK, for sequencing, genotyping, and various wet laboratory investigations to survey for evidence of evolution in response to recent or ongoing elimination measures. PDNA studies will translate genomics data on Plasmodium diversity into evidence to be shared with the sub-Saharan Ministries of Health; national malaria control programs; regional and international health authorities, such as the Africa Bureau of the World Health Organization (WHO) and the WHO global malaria program; and other stakeholders (Fig. 3).

Pooled analysis of data will provide larger diversity in sub-Saharan Africa. Each site collected 100 leukocyte-depleted P. falciparum-infected blood samples. DNA was extracted and shipped to the Wellcome Trust Sanger Institute for whole-genome sequencing, and data analysis is under way with support from the MalariaGEN resource center. As the new K37 propeller polymorphisms have been described as a molecular marker for artemisinin resistance (7), we have also been investigating their presence and prevalence in each of our African sites. Within weeks, each PDNA site collected, processed, and shipped genomic DNA or dried blood spots for sequencing. Together, these projects show how a coordinated network of African scientists can mount a rapid surveillance response.

The institutions involved in PDNA are at different levels of scientific expertise, and hence, a priority will be to engage in training and capacity-development at each participating institution for knowledge as well as ethics. Although the primary focus of the PDNA project is Plasmodium, the process of obtaining parasite DNA involves the collection of blood samples from human volunteers. Thus, in accordance with international ethical guidelines, voluntary informed consent of research participants is sought in each of the projects, and all PDNA research proposals are submitted to relevant ethics committees for review and approval.

FIG. 2. COUNTRIES REPRESENTED BY THE PLASMODIUM DIVERSITY NETWORK AFRICA MEMBERS

The PDNA represents an African initiative for the assessment of endemic-country malaria parasite diversity at the genotype and phenotype levels to address scientific questions most relevant to the successful elimination of malaria in sub-Saharan Africa. PDNA will use its range of scientific, geographic, epidemiologic, political and ethno-linguistic diversity to engage local and international stakeholders, including health policy decision-makers, to ensure that we contribute directly to the global agenda for malaria elimination.

REFERENCES AND NOTES

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SUPPLEMENTARY MATERIALS
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Table S1
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