

Embargo 22 August 2019 19:00 BST / 14:00 ET (TBC)

MALARIA CONTROL SUCCESS IN AFRICA AT RISK FROM SPREAD OF MULTI-DRUG RESISTANCE

In the first continent-wide genomic study of malaria parasites in Africa, scientists have uncovered genetic differences in some strains of the deadliest malaria parasite that enable them to develop resistance to combinations of antimalarial drugs. Researchers found populations of *Plasmodium falciparum* parasites that are distinct to certain regions in Africa, discovering genetic information that confers resistance to anti-malarial drugs in parasites that originated in Africa and which is moving between regions in all directions, putting previous success in controlling malaria at risk.

The research, published today (22 August TBC) in *Science*, comes from the first network of African scientists, the Plasmodium Diversity Network Africa (PDNA), to work with genomic tools to study the diversity of malaria parasites across the continent. In collaboration with the Wellcome Sanger Institute, the researchers studied the genetic diversity of *P. falciparum* populations endemic to several countries in sub-Saharan Africa, including Ethiopia and Ghana. Genomic surveillance data will help to track the emergence and spread of drug-resistant strains, assisting efforts to eliminate malaria.

Malaria remains a global problem, with the deadliest parasite species *P. falciparum* prevalent across sub-Saharan Africa. Between 2000 and 2015, an ongoing drive to eliminate the disease has seen worldwide malaria deaths halve from 864,000 to 429,000 per year. In 2015, 92 per cent of global malaria deaths were in Africa, with 74 per cent of these occurring in children under five years of age. * But the findings of a new study suggest this progress may be at risk if new forms of treatment aren't developed.

Previous research suggested *P. falciparum* parasites in sub-Saharan Africa were genetically similar, or homogenous, and that the flow of genes in this pathogen was always east to west, with resistance to antimalarial drugs believed to originate in south East Asia.

The results of this new study indicate, however, that *P. falciparum* parasites are genetically distinct according to which region of Africa they are found. Furthermore, researchers found that these regional populations are sharing genetic material in all directions – including genes that can confer resistance to antimalarial drugs, with drug resistance originating independently in Africa. It is thought human migration, including that resulting from colonial activity, has played a part in the evolution of *P. falciparum* in Africa.

Samples of *P. falciparum* were collected from 15 African countries by PDNA and their genetic codes sequenced at the Wellcome Sanger Institute. These genomes, along with open-source sequence data from MalariaGEN**, were analysed to trace ancestral connectivity between the various parasite populations.

Professor Abdoulaye Djimdé, Wellcome International Fellow at the Wellcome Sanger Institute and Chief of the Molecular Epidemiology and Drug Resistance Unit at the Malaria Research and Training Centre, University of Bamako, said: “Contrary to previous studies, we identified distinct Western, Central and Eastern populations of *P. falciparum*, as well as a highly-divergent Ethiopian population. Genetic material originating from all directions was shared by all populations, indicating that the flow of genes is multi-directional, as opposed to unidirectional from east to west as previously thought. This is crucial information for understanding how resistance to malaria drugs is developing in Africa.”

Researchers noted the fact that the Ethiopian parasite population is highly-differentiated from those in the rest of Africa, which suggested the ancestry of malaria parasites may have been influenced by human migration. The human population in Ethiopia also has a distinct ancestry to others in Africa, suggesting that the lack of colonization of the country might

explain its outlier status. By contrast, parasites from distant former French colonies share genetic material.

The results confirmed that populations of *P. falciparum* have shared genetic information over time, particularly genes associated with resistance to antimalarial drugs.

Most concerningly, strong genetic signatures were detected on chromosome 12 in *P. falciparum* samples from Ghana and Malawi that suggest recent evolution of the parasite could compromise the effectiveness of artemisinin-based combination therapies (ACTs). ACTs combine multiple antimalarial drugs in one treatment to overcome resistance to one or more individual drugs.

Dr Alfred Amambua-Ngwa, first author of the study, a Wellcome International Fellow at the Wellcome Sanger Institute and Assistant Professor at the Medical Research Council Unit The Gambia, London School of Hygiene and Tropical Medicine, said: "Whatever the historic factors affecting the flow of genes between the distinct *P. falciparum* populations, the multi-directional flow we've identified raises the prospect of continental spread of resistance to artemisinin-based combination therapies, which could arise from anywhere in Africa. Genomic surveillance, and on a large scale, is going to be vital to track the emergence and spread of resistance to combination therapies."

The establishment of the PDNA is an important step in continuing to track the spread of drug-resistant malaria in Africa at a crucial time, when efforts to eliminate the disease are now stalling and the prospect of multi-drug resistant strains of *P. falciparum* in Africa on the horizon.

Professor Dominic Kwiatkowski, Head of the Parasites and Microbes Programme at the Wellcome Sanger Institute and Director of the Centre for Genomics and Global Health at the University of Oxford, said: "Back in 2013, African scientists recognised the need to form a network to genomically survey pathogens like *P. falciparum* to make sure we are keeping on top of malaria as it evolves. Given the logistical challenges of travel and communication in the continent, the team have done an amazing job to work out how to conduct this research, collect the samples and analyse them to produce crucial insights into populations and drug-resistant strains. The findings are important, clearly, but I think the importance of this network in continuing the fight against malaria in Africa is not to be underestimated."

ENDS

Contact details:

Dr Matthew Midgley
Press Office
Wellcome Sanger Institute
Cambridge, CB10 1SA
Phone: 01223 494856
Email: press.office@sanger.ac.uk

Notes to Editors:

*For more information on these figures and the state of malaria in general, see the WHO World Malaria Report 2016 <https://www.who.int/malaria/media/world-malaria-report-2016/en/>

**For more information on The Malaria Genomic Epidemiology Network (MalariaGEN), visit <https://www.malariagen.net/about>

Funding:

This project was supported by the African Academy of Sciences (AAS), New

Partnership for Africa's Development Planning and Coordinating Agency (NEPAD Agency), and Wellcome. For full funding information, please refer to the full study.

Selected websites:

MalariaGEN

The Malaria Genomic Epidemiology Network (MalariaGEN) is an international community of researchers working to understand how genetic variation in humans, *Plasmodium* parasites, and *Anopheles* mosquitoes affects the biology and epidemiology of malaria, and using this knowledge to develop more effective ways to control the disease. Find out more at <https://www.malariagen.net/about>

About MRC Unit The Gambia at LSHTM

The MRC Unit The Gambia at LSHTM is one of two research units established in sub-Saharan Africa by the Medical Research Council UK and is the MRC Unit The Gambia at LSHTM's single largest investment in medical research in a low and middle income country. MRC Unit The Gambia at LSHTM represents a unique concentration of scientific expertise and high quality research platforms in the West African region.

The Unit's investigator-led research is underpinned by the combination of excellent laboratory facilities and easy access to the field with well-defined populations that are highly supportive of our research, excellent clinical services, rigorous ethical procedures and ability to deliver GCP-compliant clinical trials. Our large research portfolio spans basic research to the evaluation of interventions for the control of diseases of public health importance in sub-Saharan Africa. <https://www.mrc.gm/about-us/>

About University of Science, Techniques and Technologies of Bamako, Mali

The Malaria Research and Training Center (MRTC) within the University of Science, Techniques and Technologies of Bamako, is a renowned African-led research institution which is divided into six research units, including the Genomics and Molecular Epidemiology Unit, B-cell Laboratory within Immunology Group, Cellular immunology laboratory within Immunology Group, Molecular Epidemiology and Drug Resistance Unit, Clinical Laboratory, Data Management and Analysis Group, and Diagnostic Laboratory. During the past 20 years, MRTC in collaboration with NIH, University of Maryland, EDCTP, Wellcome, African Academy of Sciences, WHO and others has built a state-of-the-art facility including parasite culture facilities, Insectaries, genomic data storage and Bioinformatics facilities. There are five established clinical trial sites for vaccine and seven for drug trials and epidemiological studies and numerous satellite field research sites.

About MRC CGGH

The Wellcome Sanger Institute

The Wellcome Sanger Institute is a world leading genomics research centre. We undertake large-scale research that forms the foundations of knowledge in biology and medicine. We are open and collaborative; our data, results, tools and technologies are shared across the globe to advance science. Our ambition is vast – we take on projects that are not possible anywhere else. We use the power of genome sequencing to understand and harness the information in DNA. Funded by Wellcome, we have the freedom and support to push the boundaries of genomics. Our findings are used to improve health and to understand life on Earth. Find out more at www.sanger.ac.uk or follow us on [Twitter](#), [Facebook](#), [LinkedIn](#) and [on our Blog](#).

About Wellcome

Wellcome exists to improve health by helping great ideas to thrive. We support researchers, we take on big health challenges, we campaign for better science, and we help everyone get

involved with science and health research. We are a politically and financially independent foundation.