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Analyses of Malaria Parasite Transcriptomes Reveal Mechanisms Underlying Parasite Transmission and Responses to Antimalarial Drug

University of Maryland School of Medicine Scientists Develop Novel Genomic Approaches to Study the Human Pathogen Plasmodium vivax

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Plasmodium vivax, a single-celled parasite transmitted by mosquitoes, is the most widespread human malaria parasite, responsible for more than 8.5 million clinical malaria cases worldwide and threatening more than 2 billion people in 90 countries. In contrast to *P. falciparum*, it cannot be cultured in vitro and remains poorly understood and resilient to elimination efforts.

Genome sequencing studies have provided unique insights on this neglected human parasite but are limited to identifying biological differences encoded in the DNA sequence. Gene expression studies, which could provide information on the regulation of the parasite life cycle and its response to drugs, have been challenging to implement for this pathogen due to the heterogeneous mixture of parasite stages present in every patient's infection.

Now, University of Maryland School of Medicine (UMSOM) researchers teamed with researchers at the Institut Pasteur in Cambodia to analyze the parasite gene expression profiles from vivax malaria patients enrolled in a chloroquine efficacy study. Using a combination of genomic and bioinformatic approaches, they compared the parasite transcriptomes from different patient infections and described how the parasites responded to chloroquine, a common antimalarial drug.

The research was published today in *Nature Communications*.

“By analyzing the parasite mRNAs, or their transcriptomes, directly from infected patient blood samples, we were able to observe that not all infections contained the same proportion of the male and female parasites that are required for infecting mosquitoes and propagating the disease. This observation suggests that parasite transmission is more complex than we previously thought and, perhaps, that the parasite is able to modify its development to ensure optimal survival,” said David Serre, PhD, associate professor of microbiology and immunology and a member of the Institute for Genome Sciences (IGS) at UMSOM. “We also analyzed the gene expression changes induced by chloroquine treatment and demonstrated that this antimalarial drug, while efficiently eliminating *P. vivax* parasites, acts differently than it does on *P. falciparum* parasites. This emphasizes the biological differences between these two human malaria parasites



and the importance to specifically study this important pathogen if we hope to eventually eliminate malaria worldwide”.

Drs. Kim and Serre at IGS, collaborated with Drs. Popovici and Menard at the Malaria Molecular Epidemiology Unit at the Institut Pasteur in Cambodia.

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About the University of Maryland School of Medicine

The University of Maryland School of Medicine was chartered in 1807 and is the first public medical school in the United States and continues today as an innovative leader in accelerating innovation and discovery in medicine. The School of Medicine is the founding school of the University of Maryland and is an integral part of the 11-campus University System of Maryland. Located on the University of Maryland’s Baltimore campus, the School of Medicine works closely with the University of Maryland Medical Center and Medical System to provide a research-intensive, academic and clinically based education. With 43 academic departments, centers and institutes, and a faculty of more than 3,000 physicians and research scientists and more than \$400 million in extramural funding, the School is regarded as one of the leading biomedical research institutions in the U.S. with top-tier faculty and programs in cancer, brain science, surgery and transplantation, trauma and emergency medicine, vaccine development and human genomics, among other centers of excellence. The School is not only concerned with the health of the citizens of Maryland and the nation, but also has a global presence, with research and treatment facilities in more than 35 countries around the world.

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About the Institute for Genome Sciences

The Institute for Genome Sciences, founded in 2007, is an international research center within the University of Maryland School of Medicine. Comprised of an interdisciplinary, multidepartment team of investigators, the Institute uses the powerful tools of genomics and bioinformatics to understand genome function in health and disease, to study molecular and cellular networks in a variety of model systems, and to generate data and bioinformatics resources of value to the international scientific community.

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