

AMD Projects

Innovate • Transform • Protect

CDC's Advanced Molecular Detection (AMD) initiative fosters scientific innovation in genomic sequencing, epidemiology, and bioinformatics to transform public health and protect people from disease threats.

AMD Project: Next-generation Malaria Methods

Replacing outdated malaria drug resistance screening methods with next-generation molecular tools and techniques

The *Plasmodium* parasite that causes malaria continuously evolves ways to counter anti-malarial drugs. Malaria control efforts based on the use of chloroquine faltered in the 1960s when drug-resistant *Plasmodium falciparum* parasites evolved. Other malaria drug regimens—such as sulfadoxine-pyrimethamine and mefloquine—also failed in many regions due to emergence of resistance. Recently, resistance to current first-line treatments—known as artemisinin-based combination therapies—has emerged in Southeast Asia. A serious concern is the potential spread of these resistant parasites to other regions.

In addition to hampering malaria control efforts in countries where malaria is common, resistance complicates treatment of patients who have returned to the US after being infected overseas.



Emergency department staff evaluates a patient with fever who recently traveled to a malaria-endemic country. Malaria should be considered a potential medical emergency and be treated accordingly. Delay in diagnosis and treatment is a leading cause of death in malaria patients in the U.S.



Molecular markers associated with resistance to anti-malarial drugs can help detect resistant parasites. CDC uses conventional molecular tools for characterizing molecular markers, but these are cumbersome, slow, and expensive. Highly sensitive, efficient, and integrated surveillance methods will improve identification of established and emerging drug-resistant strains and allow CDC to respond rapidly to changes needed in case management and control.

CDC is developing next generation sequencing methods to detect resistant parasites rapidly. These methods will allow CDC to detect even a small number of resistant parasites present. Early identification of low levels of resistant parasites will make it easier and faster to choose the right drugs for treatment than current practices allow.

Once the new advanced molecular detection methods are fully developed and integrated, they will replace the slower and less sensitive methods now in use.

For more information on the *Plasmodium* parasite that causes malaria, please visit www.cdc.gov/malaria.



2016 Update

During the first two years of this project, investigators developed an advanced molecular detection (AMD) method to characterize and analyze drug resistance genes in *Plasmodium falciparum*, the deadliest of the four parasite species to cause human malaria. Using next generation sequencing (NGS), researchers developed a protocol for sequencing two important drug resistance genes that are associated with artemisinin and atovaquone resistance, two front-line antimalarial treatments.

In addition to NGS protocols, researchers developed two standardized and automated analysis pipelines, Malaria Drug Resistance Tracker (MDR-T) and Malaria Drug Resistance Identifier (MDR-I), to rapidly track previously known resistance mutations and identify new resistance-associated mutations.

As work on this project continues, investigators will further develop and optimize the AMD methods to include all relevant malaria drug resistance genes in a single NGS pipeline. Once fully developed and validated, these AMD methods can be used routinely for molecular surveillance of malaria drug resistance in imported malaria cases in the U.S., as well as international projects supported by CDC. These new methods detect mutations for drug resistance faster and are able to identify minor mutations more accurately than previously used methods. This work will result in a robust and efficient molecular surveillance method for tracking drug resistant malaria parasites.