Genetic markers offer new clues about how malaria mosquitoes evade eradication (w/ Video)

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The development and first use of a high-density SNP array for the malaria vector mosquito have established 400,000 genetic markers capable of revealing new insights into how the insect adapts to outsmart insecticides and other preventive measures, according to findings published in the current edition of the journal *Science*. The SNP array's snapshot of the *Anopheles gambiae* genome can be used by scientists worldwide to advance public health efforts to contain and eliminate the deadly disease, according to Boston College biologist and senior author Marc A.T. Muskavitch.

The SNP array, a technology used to examine hundreds of thousands of features within DNA, detects single nucleotide polymorphisms and establishes genetic markers that can be used to understand the entire genome, particularly with respect to disease susceptibility and the likely success of insecticides and other mosquito-targeted interventions.

"We have developed a set of 400,000 markers with which we can study the genetics of the malaria vector mosquito Anopheles gambiae," said Muskavitch, the DeLuca Professor of Biology at Boston College, who co-authored the paper with an international team of researchers. "Each marker is like a genetic signpost along the genome. These markers have revealed that when mosquito populations begin to separate from each other, it is a very complicated process that can involve hundreds of genes. The genes we have identified are genes that we can now

investigate, to better understand their roles in the complexity of mosquito populations."

The malaria mosquito is a member of a complex of seven species of mosquitoes, and within that complex are multiple populations that can display different traits and behaviors. Over many decades, modern public health efforts have sought to stop these mosquitoes, which spread the malaria parasite by taking blood meals from humans. Insecticides have been found to lose their effectiveness when the insects develop resistance to them. Muskavitch says the SNP array will yield powerful new scientific insights into these changes, which can support public health efforts in sub-Saharan Africa, where the disease is most prevalent, and elsewhere throughout the world.

"Our best tools for stopping vector mosquitoes that transmit malaria depend on mosquitoes that bite us at night when we are asleep and then rest inside our dwellings after they take our blood," Muskavitch said. "But we have already seen that mosquitoes are changing. They are beginning to bite during the day, or to rest outside. By using the SNP array, we can begin to understand the genes that lead to these differences in behavior."

He added, "Over the past 10 years, efforts on an international scale to improve the control of malaria and eliminate it have intensified. Health efforts on the ground involve the distribution of interventions. But because mosquitoes can outsmart insecticide-based interventions, we need to inform the use of those interventions with scientific insights into the genomics of vector mosquitoes."

The team - which included researchers from Boston College, the Broad Institute, Imperial College London, the University of Notre Dame, Harvard University and the Malaria Research and Training Center in Mali - designed the *Anopheles gambiae* (AG) SNP1 Array in

collaboration with Santa Clara, California-based Affymetrix. The array features 400,000 SNPs from among the 3 million found in four sequenced strains of *Anopheles gambiae*, which provides an immensely higher resolution than the 42- and 1,536-marker sets previously available to malaria vector biologists.

Muskavitch said the development of the array is an essential advance for researchers working toward the goal of eradicating malaria, which has been set forth by the Bill and Melinda Gates Foundation, a leading funder of malaria research.

"By obtaining insights into the genetic changes that underlie the adaptations of mosquitoes to evade our interventions, we have a better chance of making sure that mosquitoes can be controlled," Muskavitch said. "The development of this array depended critically on working with African colleagues who understand the transmission of malaria and work to control it in their home countries. Now that we have established this approach for *Anopheles gambiae*, we are beginning to work with even more scientists in Africa who are working to understand and control the mosquitoes that transmit this deadly disease."

Provided by Boston College