Genetic make-up of children explains how they fight malaria infection

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Researchers from Sainte-Justine University Hospital Center and University of Montreal have identified several novel genes that make some children more efficient than others in the way their immune system responds to malaria infection. This world-first in integrative efforts to track down genes predisposing to specific immune responses to malaria and ultimately to identify the most suitable targets for vaccines or treatments was published in the *Proceedings of the National Academy of Sciences* by lead author Dr. Youssef Idaghdour and senior author Pr. Philip Awadalla, whose laboratory has been performing world-wide malaria research for the past 13 years.

"Malaria is a major health problem world-wide, with over 3 billion individuals at risk and hundreds of thousands of deaths annually, a majority of which are African children under the age of 5. Why are some children prone to infection, while others are resistant and efficiently fight the disease? These are the questions we sought to answer with our study", Idaghdour says.

However, to succeed where many other studies have failed, the team used an approach different from the classic in vitro one, where the genome is analyzed using cells grown in a laboratory. Instead, they used an in vivo approach, analyzing blood samples of children from the Republic of Benin, West Africa, collected with the help of collaborators in the city of Cotonou and the nearby village of Zinvié. "This approach allowed us to identify how the "environment" engages in an arms race to define the clinical course of the disease, in this case the environment

being the number of parasites detected in the child's blood running against the genetic make-up of the infected child", Idaghdour explains.

"We used an innovative combination of technologies that assessed both genetic variation among children and the conditions in which their genes are "expressed". By doing so, we increased the power of our analysis by permitting us not only to detect the mutations, but also to capture their effect depending on how they affect genes being turned "on" or "off" in presence of the parasite", Awadalla explains. "Our approach made us successful, where million-dollar studies have failed in the past. There has never been this many genes associated with malaria discovered in one study."

This major milestone in understanding how the genetic profile affects the ability of children to cope with infection could pave the way to the development of low-cost genetic profiling tests in a not so far future. "Accurate diagnosis of the infectious agent is critical for appropriate treatment, of course. However, determining a patient's genetic predisposition to infection would allow us to be more aggressive in our treatment of patients, whether we are speaking of vaccines or preventive drugs", Awadalla says.

Provided by University of Montreal