Duffy-negative blood types no longer protected from P. Vivax malaria

March 15 2010

In a paradigm changing discovery, *Plasmodium vivax* (*P. vivax*) malaria has been identified in a population historically thought to be resistant to the disease, those who do not express the Duffy blood group protein on their red blood cells, according to researchers from Case Western Reserve University School of Medicine, Pasteur Institute, and the Madagascar Ministry of Health. In a study of more than 600 individuals from eight communities covering the main malaria transmission areas of Madagascar, the researchers found that 10 percent of people experiencing clinical malaria were Duffy-negative and infected with *P. vivax*. These findings were published in an upcoming issue of the *Proceedings of the National Academy of Sciences*.

Since the early 1920s, it has been widely accepted that people of African ancestry are resistant to *P. vivax* blood-stage infection and clinical malaria. The Duffy-negative blood group, one of the more than 30 blood types, is predominant in most African ethnic groups. In recent years, researchers have begun to suspect that *P. vivax*, the world's most abundant malaria parasite, had made its way into the blood of Duffy-negative people, but until now, confirming evidence that the parasite had entered the red blood cells remained elusive.

The Case Western Reserve-Pasteur Institute team has documented their novel discovery with the first photographic evidence of the parasite's presence within red blood cells of many Duffy-negative people experiencing malarial illness. It is understood that those with this blood type, can have *P. vivax* living dormant in their liver cells where it does

not make people sick. What has distinguished Duffy-negatives from all others was that the malaria parasite was unable to cross the threshold from liver cells to blood cells. The lynchpin responsible for resistance to vivax malaria has been that when the Duffy antigen is missing the parasite is not able to invade the red blood cell and cause disease.

"The study confirms that *P. vivax* is not dependent on the Duffy antigen for establishing blood-stage infection and disease in Madagascar. Evolution of new parasite strains, infiltrating a new group of people who are Duffy-negative, seems to be occurring within a population of people from different ethnic backgrounds," says Peter A. Zimmerman, Ph.D., the study's senior author and Professor of International Health, Genetics and Biology in the Center for Global Health and Diseases at Case Western Reserve University School of Medicine. "These findings will have a major impact on efforts to eliminate malaria worldwide, particularly in large regions of Duffy-negative west, central and southern Africa."

The study's findings suggest that population mixing on the island of Madagascar increases the Duffy-negative's susceptibility to *P. vivax*. With ancestors of both Duffy-negative Africa and Duffy-positive Southeast Asia in Madagascar, *P. vivax* has steady opportunity to attempt infection of Duffy-negative red blood cells. Through these opportunities, and the lifecycle necessity of blood-stage infection, *P. vivax* strains in Madagascar may be optimizing an otherwise cryptic invasion pathway.

Malaria, one of the world's "big three" diseases, is a major health problem. Forty percent of the world's 6.5 billion people live in areas where malaria transmission occurs. As many as three million people are diagnosed with new cases of *P. vivax* malaria each year, which is one of the four types of malaria. "It will be imperative for the global health community to find ways to prevent the spread of these new strains of *P. vivax* to the continent of Africa," says Dr. Zimmerman.

In Madagascar, malaria is endemic to more than three-quarters of the island. With almost one million clinical cases reported each year, this disease is a major public health problem. Major efforts to fight malaria are focused on Plasmodium falciparum. While *P. vivax* is the second most prevalent malaria parasite, public health data on it is limited. "We did not anticipate such a widespread phenomenon when we started the study with our Malagasy colleagues from the National Malaria Control Programme. Finding vivax malaria in a group previously considered resistant adds yet another public health threat to this population. It was bad news. We need to understand how the parasite has evolved in Madagascar to spread disease to a broader population," says Dr. Didier Ménard from Pasteur Institute.

Dr. Odile Mercereau-Puijalon, Head of the Parasite Molecular Immunology Unit at the Pasteur Institute, commented, "The large numbers of *P. vivax* parasitized red blood cells in Duffy-negative patients shows an efficient invasion process in cells considered to be resistant to infection. This capacity is clearly not restricted to a single *P. vivax* strain in Madagascar and is a widespread phenomenon across the island. Our findings illustrate the extraordinary capacity of malaria parasites to overcome barriers. This calls for increased vigilance in the efforts to control malaria."

With these novel findings, the Case Western Reserve and Pasteur Institute researchers will examine how the malaria parasites successfully invade the cells and determine the molecular receptor involved in this process. Through their future studies the team hopes to determine how these parasites invade red blood cells and contribute to development of an effective vaccine against vivax malaria.

Provided by Case Western Reserve University