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The malaria parasite 'P. vivax' can remain in the spleen upon expression of certain proteins

This could represent an additional challenge for eliminating the parasite

The malaria parasite *Plasmodium vivax* can **adhere to human spleen cells through the expression of so-called variant proteins**. These are the conclusions of a study led by the Barcelona Institute for Global health (ISGlobal), an institution supported by "la Caixa" and the Germans Trias i Pujol Institute (IGTP). The results, published in Proceedings of the National Academy of Sciences (PNAS), suggest that this could represent an additional challenge to eliminating the disease.

Malaria by *P. vivax* is the most widespread form of the disease outside the African continent and is responsible for 7.5 million cases every year. Even if it is considered les lethal than *P. falciparum* malaria, it can cause severe symptoms and even death. One of the enigmas of *P. vivax infection* is its capacity to cause severe symptoms despite low levels of parasites circulating in the blood. Recent studies suggest this could be due to the **parasite 'hiding' in the spleen**, challenging the dogma that the organ's sole function is to eliminate red blood cells infected by the parasite.

In this study, the team led by Carmen Fernandez-Becerra and Hernando A del Portillo investigated the spleen's role in *P. vivax* infection. To do so, they infected monkeys that lacked - or not - a spleen, and compared the expression of over 5,000 genes in parasites recovered from these animals. They identified **67 genes that were only expressed in the presence of a spleen**. Most of these genes belonged to variant protein families. The authors then showed that **one of the genes belonging to the VIR family promotes parasite adherence to human spleen cells**, but not to lung cells. The authors also demonstrated that these proteins are recognised by our immune system. They found antibodies against these proteins in serum samples from 383 children from Papua New Guinea diagnosed with the disease. Moreover, antibodies against one of these proteins (HYP1) were associated with protection against clinical episodes during the follow-up period.

"These results suggest that **the spleen plays a double role in malaria pathology**," explains Hernando A del Portillo, ICREA researcher at ISGlobal. "On one hand, it destroys infected red blood cells; on the other hand, it represents a niche where infected red blood cells can adhere, thereby explaining the low number of circulating parasites in malaria vivax. These findings can also help us **find new vaccine targets and exposure markers**," he adds.

"This also means that, together with the bone marrow, the spleen is another organ where the parasite can hide, thereby challenging the elimination of these cryptic infections," says Carmen Fernández-Becerra, first author of the study.

Reference

Fernandez-Becerra C, Bernabeu M, Castellanos A, et al. Plasmodium vivax spleen-dependent genes encode antigens associated with cythoadhesion and clinical protection. PNAS doi:10.1073/pnas.1920596117

About ISGlobal

The Barcelona Institute for Global Health, ISGlobal, is the fruit of an innovative alliance between the "la Caixa" Foundation and academic and government institutions to contribute to the efforts undertaken by the international community to address the challenges in global health. ISGlobal is a consolidated hub of excellence in research that has grown out of work first started in the world of health care by the Hospital Clínic and the Parc de Salut MAR and in the academic sphere by the University of Barcelona and Pompeu Fabra University. The pivotal mechanism of its work model is the transfer of knowledge generated by scientific research to practice, a task undertaken by the institute's Education and Policy and Global Development departments. ISGlobal has been named a Severo Ochoa Centre of Excellence and is a member of the CERCA programme of the Generalitat de Catalunya.

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