MedicalXpress

The first genes for susceptibility to cerebral malaria in Angolan children identified

June 16 2010

Malaria, caused by the parasite *Plasmodium falciparum*, remains one of the main causes of death worldwide. An international team of researchers lead by Instituto Gulbenkian de Ciência, IGC, scientist Carlos Penha-Gonçalves, has identified the first genetic risk factors for the development of cerebral malaria in Angolan children, a severe manifestation of malaria infection. These findings, just published in the journal *Plos One*, are the outcome of a study carried out at a pediatrics hospital in Luanda, an Angolan province where malaria is the first cause of morbidity and mortality.

It is known that genetic factors influence how humans react to infection by the parasite Plasmodium falciparum, leading some to develop uncomplicated disease, and others to develop severe manifestations, such as cerebral malaria (CM), an acute and life threatening complication of clinical malaria. However, little was known about genetic factors that increase susceptibility to specific malaria complications. Carlos Penha-Gonçalves and his team compared a host of genetic variations between CM patients and infected patients that did not manifest a CM outcome. Starting from a list of candidate genes, they identified variants in two genes, TGFB2 and HMOX, that appear to contribute to the development of CM in Angolan children. Carriers of these variants are thus at a greater risk of developing cerebral malaria, if infected with the Plasmodium.

Both these genes have been previously implicated in CM and other forms of severe malaria in mouse models artificially infected with

malaria in the laboratory. This study now reveals their relevance to humans, too.

Rosário Sambo, a PhD student in the group and first author of the paper, describes how the study was carried out, "We enrolled a total of 749 children and their mothers, living in Luanda, in this study. The children were between 6 months and 13 years old, all attending the city's main paediatric hospital. This group included healthy children, cerebral malaria patients, children with severe malaria (but not cerebral malaria), and patients with uncomplicated malaria. Using genetic mapping techniques, we looked at variations in the DNA sequences of several genes, including TGFB2 and HMOX1, and investigated how they were represented amongst patients in each of the groups".

Says Carlos Penha Gonçalves, "This study provides important insights for future association and functional studies, in other populations, to determine the exact role of these genes in the development of cerebral malaria. In the future, this battery of genetic variants may be used to identify patients who are more susceptible to this severe outcome of malaria infection early, and prevent its development".

Provided by Instituto Gulbenkian de Ciencia