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A Study Identifies New Markers Associated with Protection by the RTS,S Malaria Vaccine

Infants who have been less exposed to the parasite are better protected

Barcelona, 31 October, 2018- Protection conferred by the RTS,S malaria vaccine depends greatly on the amount and subclass of antibodies generated upon vaccination, and on previous exposure levels to the parasite, according to a study led by ISGlobal, an institution supported by “la Caixa” Foundation. The results, published in *BMC Medicine*, shed new light on the mechanisms by which RTS,S confers protection and provide the basis for developing more efficacious vaccines.

Malaria elimination will require the right combination of interventions, including an effective vaccine. The RTS,S vaccine (Mosquirix™), approved by the European Medical Agency, has shown partial effectiveness – 31% in 6 to 12 weeks-old infants, and 56% in children aged 5 to 17 months. ISGlobal researcher, Carlota Dobaño, and her group, have been working over the past years to understand the reasons for this variability and identify vaccine protection correlates.

In this study, an international team led by Dobaño investigated not only the levels but also the type of antibodies induced by the vaccine, thanks to a quantitative assay developed by her group. In particular, they measured levels of antibody subclasses against different fragments of the CSP parasite protein and the Hepatitis B virus surface antigen (HBsAg), the two proteins comprised in RTS,S. They analysed serum and plasma from almost 200 infants and children from Kintampo, Ghana (an area with high malaria transmission) and Manhica, Mozambique (low malaria transmission), vaccinated during the phase 3 clinical trial for RTS,S/AS01E.

The results confirm that the vaccine induces significant levels of IgG antibodies against both proteins (CSP and HBsAg), which are higher in children than in infants. However, not all subclasses of CSP antibodies seem to protect: IgG1 and IgG3 antibodies were associated with protection, while IgG2 and IgG4 were associated with higher disease risk. “The balance between the different subclasses seems to be more important than the total IgG levels,” explains lead author Itziar Ubbillos. “This could be because IgG1 and IgG3 antibodies have the capacity to stick to the parasite and give an ‘eat-me’ signal to cells of the immune system,” she adds.

The results also indicate that children with higher pre-vaccine levels of CSP antibodies were less protected against disease, post-vaccination. “This means that the vaccine will exert a larger benefit to infants who have not been exposed to the parasite in utero or during the first weeks of life,” explains Dobaño. “This study, fruit of many years of work and many collaborators, identifies new correlates of vaccine success and failure in African children and provides a basis for designing more efficacious vaccines,” says the researcher.

Reference: Ubbillos I, Ayestaran A, Nhabomba A, et al. Baseline exposure, antibody subclass and hepatitis B response differentially affect malaria protective immunity following RTS,S/AS01E vaccination in African children. *BMC Medicine* 2018 OCT 31; 16:197. doi.org/10.1186/s12916-018-1186-4.

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About ISGlobal

The Barcelona Institute for Global Health (ISGlobal), the result of an innovative alliance between the “la Caixa” Foundation, academic institutions and government bodies, was set up to contribute to the work undertaken by the international community to address the challenges of health in a globalised world. ISGlobal is a consolidated hub of excellence based on research and health care that has grown from the work first started in the world of clinical 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 core 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 belongs to the Catalan Government’s CERCA network.

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