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Researchers reveal why malaria vaccine provides only moderate protection among vaccinated children

Published on October 23, 2015 at 6:51 AM

Using new, highly sensitive genomic sequencing technology, an international team of researchers has found new biological evidence to help explain why the malaria vaccine candidate RTS,S/AS01 (called RTS,S) provided only moderate protection among vaccinated children during clinical testing. The researchers, funded in part by the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, found that genetic variability in the surface protein targeted by the RTS,S vaccine likely played a significant role. The findings are published online today in the *New England Journal of Medicine*.

The RTS,S vaccine was designed to target the circumsporozoite (CS) protein found on the surface of malaria-causing Plasmodium parasites. However, while the CS protein is genetically diverse, meaning that it has different variants, the RTS,S vaccine incorporates only one variant. In an evaluation of blood samples from nearly 5,000 of the infants and children who participated in Phase 3 clinical testing of the vaccine, the researchers found that the RTS,S vaccine was most effective at preventing malaria in children ages 5 to 17 months infected with parasites with the same protein variant as the RTS,S vaccine, while a mismatch corresponded with a lesser degree of protection. This differential effect was not seen in blood samples from vaccinated infants ages 6 to 12 weeks.

Previous studies that have looked at the genetic variations in the CS protein did not suggest that these variations may limit or restrict vaccine protection. This new study included a larger sample size and used advanced, more sensitive genomic sequencing technology than previously available. The findings will inform future malaria vaccine development, and the genomics approach used could be applied to other infectious diseases with changing vaccine targets, according to the authors.

Source:
NIH/National Institute of Allergy and Infectious Diseases