

Naturally occurring protection against severe malaria

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In a study to be published in the next issue of the *Proceedings of the National Academy of Sciences (PNAS)*, researchers at the Instituto Gulbenkian de Ciência, in Portugal, show that an anti-oxidant drug can protect against the development of deadly forms of malaria. These findings have direct implications for the treatment of this devastating disease, caused by the parasite *Plasmodium*, and still one of the main causes of death worldwide.

The team lead by Miguel Soares had previously shown that, when *Plasmodium* multiplies inside [red blood cells](#) (the cells that transport oxygen from the lungs into tissues) it causes these cells to burst and to release hemoglobin (the protein to which oxygen binds inside red blood cells) into the blood stream. Once outside the red [blood cells](#), hemoglobin itself can release its heme groups (the four iron centres through which oxygen binds to hemoglobin), which leads to the severe symptoms of malaria and eventually to death.

Now, the researchers found that once infected by *Plasmodium*, mice express high levels of heme-oxygenase-1 (HO-1), an enzyme that degrades heme and thus protects the infected mice from developing severe forms of malaria. Furthermore, an anti-oxidant drug, N-acetylcysteine (NAC), has the same affect as HO-1, when given to *Plasmodium*-infected mice.

Miguel Soares explains, 'The antioxidant action of HO-1 is part of the host's natural defence strategy against the [malaria parasite](#). It affords a

potent protective effect against malaria but, astonishingly, does not seem to directly affect the parasite. In some cases the reaction of the host against the parasite can lead to death of the infected host. The protective mechanism afforded by HO-1 allows this host response to kill the parasite without compromising its own survival. This finding suggest that there might be alternative therapeutic approaches to treat malaria, which, unlike the current ones would not aim at killing the parasite directly, but rather at strengthening the health status of the host, so that the host could kill parasite and survive. This type therapeutic approach should provide potent protection against severe forms of malaria and thus save lives without favouring the appearance of resistant strains of Plasmodium.

'Moreover, one might be able to apply the same strategy to a range of other infectious diseases and impact on the treatment of not only malaria but a variety of other infectious diseases, a line of research we are actively pursuing at the Instituto Gulbenkian de Ciência.'

More information: Elsa Seixá, Rafaella Gozzelino, Ângelo Chora, Ana Ferreira, Gabriela Silva, Rasmus Larsen, Sofia Rebelo, Carmen Penido, R. Neal Smith, António Coutinho and Miguel P Soares (2009) Heme Oxygenase-1 affords protection against non-cerebral forms of severe malaria. *PNAS* Early Edition.

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