Alpha-tocopherol transfer protein disruption confers resistance to malarial infection in mice.

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Background: Various factors impact the severity of malaria, including the nutritional status of the host. Vitamin E, an intra and extracellular anti-oxidant, is one such nutrient whose absence was shown previously to negatively affect *Plasmodium* development. However, mechanisms of this *Plasmodium* inhibition, in addition to means by which to exploit this finding as a therapeutic strategy, remain unclear.

Methods: α-TTP knockout mice were infected with *Plasmodium berghei* NK65 or *Plasmodium yoelii* XL-17, parasitaemia, survival rate were monitored. In one part of the experiments mice were fed with a supplemented diet of vitamin E and then infected. In addition, parasite DNA damage was monitored by means of comet assay and 8-OHdG test. Moreover, infected mice were treated with chloroquine and parasitaemia and survival rate were monitored.

Results: Inhibition of α-tocopherol transfer protein (α-TTP), a determinant of vitamin E concentration in circulation, confers resistance to malarial infection as a result of oxidative damage to the parasites. Furthermore, in combination with the anti-malarial drug chloroquine results were even more dramatic.

Conclusion: Considering that these knockout mice lack observable negative impacts typical of vitamin E deficiency, these results suggest that inhibition of α-TTP activity in the liver may be a useful strategy in the prevention and treatment of malaria infection. Moreover, a combined strategy of α-TTP inhibition and chloroquine treatment might be effective against drug resistant parasites.