New hope for advances in treating malaria

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Researchers at the University of Leeds have developed chemicals which kill the most deadly malaria-causing parasite, *Plasmodium falciparum* - including those resistant to existing drugs.

The compounds work by preventing the enzyme dihydroorotate dehydrogenase (DHODH) - essential to the growth of the parasite - from working, which results in its death.

Says lead researcher Dr Glenn McConkey, from Leeds' Faculty of Biological Sciences: "Without this enzyme, *Plasmodium falciparum* is unable to grow and therefore it dies. The inhibitors developed at Leeds bind to the DHODH enzyme in the parasite and stop it functioning, preventing the proliferation of the parasites, which live in red blood cells. In addition, our chemicals are equally effective against parasites that have developed resistance to drugs."

He adds: "DHODH in humans is not an essential enzyme, so by concentrating our studies on it we can develop chemical inhibitors that have a negative impact on the parasite without any major side-effects to the human host. In effect we are exploiting a biological difference, and this will allow us to develop potent, selective inhibitors."

According to the World Health Organisation (WHO), malaria kills a million people across the globe each year, with forty per cent of the world's population at risk of contracting the disease. WHO also estimates that a child dies from malaria every 30 seconds.

Dr McConkey says: "Our chemicals are particularly exciting as they kill malaria parasites at low concentrations, something that is important for medicines as they are massively diluted on entering the bloodstream and, unlike many pharmaceutical products, we have a firm understanding of the molecular basis of their action. This project highlights the benefits of combining biological and chemistry disciplines."

Dr McConkey says the next stage of this research is to develop a larger collection of potent inhibitors and to see how these chemicals work alongside commonly used treatments.

"The parasites responsible for malaria have been very effective at developing resistance to existing drugs and efforts to find replacements are often stymied by the rate of resistance. Therefore it is essential that new products work effectively in combination with those already on the market," he says.

The research is published in the latest edition of the *Journal of Medicinal Chemistry*.

Source: University of Leeds (news : web)

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