Griseofulvin: preventing malarial infections in humans

The existing problem or issue

Malaria kills approximately 655,000 people every year. 86% of these are children. A virulent strain of malaria can kill within 24 hours. According to the World Health Organisation (WHO), approximately half of the world’s population is at risk of contracting or suffering from malaria. New infections are diagnosed at a rate of about 250 million cases each year. People living in poor countries are the most vulnerable with Africa having the highest number of infections and subsequent fatalities.

As humans are the definitive host for malarial parasites, malaria occurs wherever humans and mosquitoes coexist. In humans, four species of Plasmodium sp. cause malaria. Malaria develops as a result of multiplication of Plasmodium sp. in cells of the liver (hepatocytes) and red blood cells.

The majority of malaria drugs act on the parasite itself. An effective vaccine against malaria does not yet exist. Insecticide-treated bed nets have been valuable in reducing infections however there are concerns about the development of insecticide resistance. Artemisinin-based combination therapy is widely recommended as the most effective anti-malaria solution.

Our solution

Research has determined that host FECH is necessary to sustain a normal malaria infection in mice. Griseofulvin, an existing anti-fungal drug used to treat skin infections, has an anti-FECH activity (Bellington et al., 1995; Holley et al., 1991).

Our team has identified a pathway in the malarial parasite where the parasite uses an enzyme from the human host to help it replicate. Early trials have been conducted where a human takes Griseofulvin, has blood taken, and then their blood is infected with malarial parasites in the laboratory, are promising. Griseofulvin appears to disrupt the life cycle of the malarial parasite. A Phase I clinical trial, using human subjects, is now underway.

So, by using pharmacological agents that affect specific biochemical cascades in the host which the parasite uses as a source, we effectively can starve the parasite. Even a single dose is very effective, as almost complete inhibition is achieved after a single dose of the medicine.

Advantages

1. Inhibits parasite growth
2. Already FDA and TGA approved drug.
3. Active in vitro against drug resistant parasites.
4. Ex vivo studies indicate it could be used as a treatment.
5. Minimal side effects.

Applications

Antimalarial treatment.

Inventors

Prof. Simon Foote, A/Prof. Brendan McMorran, Dr. Clare Smith.
Intellectual Property position
PCT/AU2012/001422 "A method of treatment and prophylaxis and compositions useful therefor"

Publications
Journal manuscript in preparation.

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