Sea cucumber protein used to inhibit development of malaria parasite

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Scientists have genetically engineered a mosquito to release a sea-cucumber protein into its gut which impairs the development of malaria parasites, according to research out today (21 December) in *PLoS Pathogens*. Researchers say this development is a step towards developing future methods of preventing the transmission of malaria.

Malaria is caused by parasites whose lives begin in the bodies of mosquitoes. When mosquitoes feed on the blood of an infected human, the malaria parasites undergo complex development in the insect's gut. The new study has focused on disrupting this growth and development with a lethal protein, CEL-III, found in sea cucumbers, to prevent the mosquito from passing on the parasite.

Human blood infected with malaria contains parasitic gametocytes – cells which can create parasite sperm and eggs in the gut of the insect. These then fertilise, kick-starting the parasite reproductive process and life cycle by producing invasive offspring called ookinetes.

These ookinetes then migrate through the mosquito's stomach wall and produce thousands of 'daughter' cells known as sporozoites. After 10-20 days these are ready in the salivary glands to infect another human when the mosquito takes a subsequent blood meal.

The international team fused part of the sea cucumber lectin gene with part of a mosquito gene so that the mosquito would release lectin into its gut during feeding. The released lectin is toxic to the ookinete and

therefore kills the parasite in the mosquito's stomach.

In laboratory tests the research team showed that introducing lectin to the mosquito's gut in this way significantly impaired the development of malaria parasites inside the mosquito, potentially preventing transmission to other people. Early indications suggest that this sea cucumber protein could be effective on more than one of the four different parasites that can cause malaria in humans.

Professor Bob Sinden from Imperial College London's Department of Life Sciences, one of the authors on the paper said: "These results are very promising and show that genetically engineering mosquitoes in this way has a clear impact on the parasites' ability to multiply inside the mosquito host."

However, Professor Sinden explains that there is still a lot of work to do before such techniques can be used to combat the spread of malaria in real-world scenario. This is because although the sea cucumber protein significantly reduces the number of parasites in mosquitoes, it does not totally remove all parasites from all mosquitoes and as such, at this stage of development, would not be effective enough to prevent transmission of malaria to humans.

Professor Sinden says he hopes studies such as this one, which improve scientists' understanding of the complex process by which malaria parasites are transmitted, will lead to new advances in the quest to prevent malaria.

"Ultimately, one aim of our field is to find a way of genetically engineering mosquitoes so that the malaria parasite cannot develop inside them. This study is one more step along the road towards achieving that goal, not least because it has been shown that more than one species of malaria can be killed in this way."

About 40% of the world's population are at risk of malaria. Of these 2.5 billion people at risk, more than 500 million become severely ill with malaria every year and more than 1 million die from the effects of the disease.

Malaria is especially a serious problem in Africa, where one in every five childhood deaths is due to the effects of the disease. An African child has on average between 1.6 and 5.4 episodes of malaria fever each year.

Citation: Yoshida S, Shimada Y, Kondoh D, Kouzuma Y, Ghosh AK, et al. (2007) Hemolytic C-type lectin CEL-III from sea cucumber expressed in transgenic mosquitoes impairs malaria parasite development. PLoS Pathog 3(12): e192. doi:10.1371/journal.ppat.0030192 (www.plospathogens.org)

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