Team discovers reasons for malaria's drug resistance

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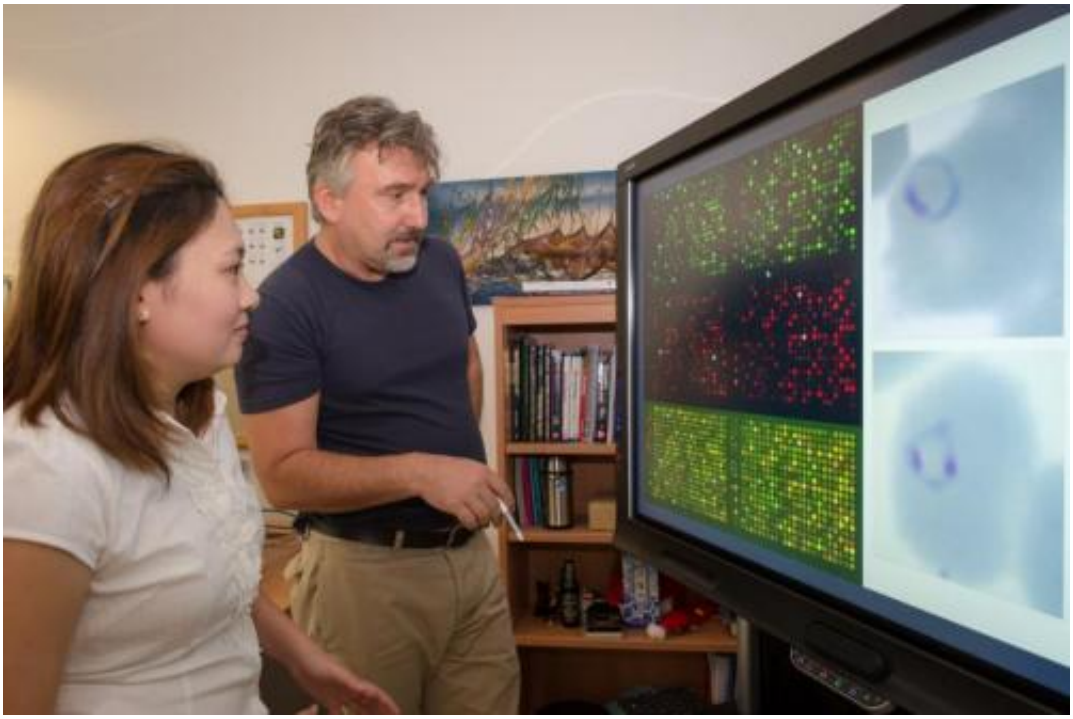

Associate professor Zbynek Bozdech (centre) discussing the microassay results (green and red) with Dr. Sachel Mok (left). Credit: NTU Singapore

Scientists from Nanyang Technological University (NTU) have discovered exactly how the malaria parasite is developing resistance towards the most important front-line drugs used to treat the disease.

Malaria is a mosquito-borne parasite which affects over 60 million

people worldwide and in serious cases, can be fatal. There is currently no viable vaccine for malaria while antimalarial drugs and prophylaxis are losing its efficacy with increasing drug resistance.

NTU Associate Professor Zbynek Bozdech, who led an international research team from 11 different countries, said knowing how the malaria parasite is developing drug resistance will help healthcare workers better treat patients suffering from malaria infections.

Their breakthrough findings are published today (12 Dec) in *Science*.

Using a cost-effective microarray technique, Prof Bozdech's team from NTU's School of Biological Sciences, analysed 1,000 malaria samples taken from patients in the area of the Greater Mekong Subregion.

The Greater Mekong Subregion includes countries such as Cambodia, Thailand, Vietnam, Laos and Myanmar, where various strains of malaria are still prevalent.

Prof Bozdech said the surprising find was that almost all the malaria parasites found in Cambodia and nearby regions had mutated and developed resistance to Artemisinin, the main drug used in combination therapies to treat malaria.

This is a stark difference when compared to malaria parasites from the Congo and other African countries. There, only one to three per cent of the malaria parasites had mutated and drug resistance has not yet been detected in the rest.

"Doctors in the Greater Mekong Subregion are finding that Artemisinin-based treatment - the wonder drug cocktail that can treat patients in three days - is now taking twice as long to work, and in some rare cases, has little to no effect," said Prof Bozdech, a biochemist and molecular

biologist.

"To find out exactly what the parasite cell is doing to protect itself against Artemisinin, we correlated the clinical data of the 1,000 samples with functional genomics results using our own customised techniques."

NTU research fellow Dr Sachel Mok, the first author of the scientific paper, said they found the malaria parasite's two major ways by which it becomes resistant to Artemisinin.

"First, the malaria parasite increased its capacity to repair the damage caused by the anti-malarial drug which gives it a higher chance of survival," said the Singaporean researcher.

"Second, because the drug is more effective against the parasite at its later stage of its development, the parasite slowed down its growth so it could survive longer in the younger stages.

"Using methods like gene expression analysis, we linked these two phenomena to a gene named K13, which was previously suggested to be associated with drug resistance but it was not clear how."

With this new knowledge, doctors will be able to design new strategies for drug treatments, particularly when deciding which cocktail of drugs will work better with Artemisinin to better treat patients.

The findings of this study will also give scientists and governments valuable data on how to better monitor the drug resistance of the malaria parasite and develop more effective ways of combating it.

Prof Bozdech, the Associate Chair for Research at NTU's School of Biological Sciences, said that overall research has shown that the drug resistance in malaria has been growing in the Greater Mekong Subregion

and is likely to spread to surrounding areas.

In addition, other researchers have shown possible cases of monkey malaria spreading to humans in nearby Asian countries. While it is not the first time malaria developed a resistance to previous drugs, Artemisinin is the last effective drug available as new drugs have yet to be developed.

"What history has shown us with the previous drugs is that even with an effective antimalarial drug, all it takes is for something to change in the malaria parasites and we will face a huge challenge trying to contain its growth again," Prof Bozdech explained.

More information: "Population transcriptomics of human malaria parasites reveals the mechanism of artemisinin resistance," by S. Mok et la. *Science*, www.sciencemag.org/lookup/doi/ … 1126/science.1260403

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