# Novel molecule prevents malaria, shows research

Researchers from New Delhi have, for the first time, deciphered a multiprotein complex that is involved in the invasion of the red blood cells (RBCs) by Plasmodium falciparum malaria parasites. They have also identified a peptide molecule that can effectively prevent the interaction between malaria parasites and receptors found on RBCs thereby preventing the parasites from invading the RBCs and causing the disease.

During infection with Plasmodium species, the parasite invades RBCs and replicates inside them. It is during the blood stage of infection that malaria disease occurs.

P. falciparum parasites are known to quickly develop resistance against drugs through mutations. A team led by Dr. Anand Ranganathan from the Special Centre for Molecular Medicine at Jawaharlal Nehru University (JNU), New Delhi and Dr. Pawan Malhotra from the International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi has used a different approach to overcome the problem of drug resistance.

Instead of targeting the parasite, the molecule targets a specific receptor — cyclophilin B — found on the surface of RBCs that are used by the parasites to bind and invade them. Since the peptide molecule binds to cyclophilin B receptors, the parasites are unable to bind to receptors and invade the cells.

In experiments carried out in test tubes, there was about 80% reduction in parasite invasion of RBCs.

“Unlike the malaria parasites, the red blood cell receptors will not undergo mutation. That is why we were able to target the receptors and prevent the invasion of RBCs by even the drug-resistant malaria parasites,” says Dr. Ranganathan.

An immunosuppressive drug (cyclosporine A) that binds to cyclophilin B receptors on RBCs is effective in killing malaria parasites. “But in mice model it has been shown that the drug has adverse effects as it also kills RBCs. Using the drug in two different experiments we confirmed that cyclophilin B receptors were involved in the invasion process,” says Dr. Prem Prakash from ICGEB and the first author of the paper published in Nature Communications.

“We found multiple sets of interactions between parasites and human RBCs,” says Dr. Mohammad Zeeshan from ICGEB and the other first author of the paper. There are two main receptors on RBCs and two parasite proteins which form a four-protein complex.

“By interrupting the binding of the parasite protein with RBCs at one of the receptors the whole protein complex falls apart. It is like a number lock with a four-digit combination. Interrupting any one of the steps will prevent the parasite invasion of RBCs,” says Dr. Ranganathan.

Having deciphered the mechanism of parasite entry, the team is now working to reduce the dosage to use the peptide as a drug. “We can either modify the cyclosporine A drug to make it less toxic and use it for preventing malaria or use the peptide as an inhibitor. It is easier to take the drug than the peptide to clinical testing by making necessary modifications,” says Dr. Malhotra.

Tux brushing tussar, cards being exchanged like cocaine packets, billionaires mingled at Illuminating India

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