## Life Sciences 2015



Battling malaria and staying ahead of evolution

"My area of research is understanding the malaria parasite functions, how it invades the human cells and how it survives within the human cells and how it utilizes its protein motors to cause infection in human hosts. We use structural biology to understand these proteins and then the structural biology insights can provide new avenues for drug and vaccine development."

## Amit Sharma

Head, Structural and Computational Biology Group, International Centre for Genetic Engineering and Biotechnology, New Delhi

- Ph. D. in Protein Crystallography from Northwestern University, Evanston
- Junior Research Fellow, University of Oxford

Dr. Amit Sharma studies the fundamental science of malaria, one of the most insidious diseases worldwide. He has carried out crystal structure determinations of proteins in the field of crystallographic instrumentation with an international network of innovators. Sharma has advanced structural biology and worked at the frontiers of basic science to solve major medical problems in infectious diseases.





Experts estimate that malaria is responsible for half of all human deaths since the Stone Age. According to a recent WHO report around 3.2 billion people worldwide are at risk from malaria. That is approximately half the world's population. In 2015, there were 214 million cases of malaria. and an estimated 438,000 of those lost their lives to this disease. Malaria has its origins in prehistory as a disease that most probably infected primates in Africa before jumping to humans. At its peak it manifested in every continent except Antarctica.



develop drugs to treat malaria at least since the 19th century when the malarial parasite Plasmodium was first identified as the cause of malaria. Dr. Amit Sharma is a structural biologist who works on the malarial parasite. Sharma and his team study the molecular structure of the proteins found in the parasite. They have been attempting to decipher the molecular structure of key proteins involved in the biology of pathogenesis of the malarial parasite.

Pathogens such as the malarial parasite have evolved over the past 100 million years to invade host cells in humans and other animal cells. As with all life forms on earth, they have specific proteins that allow them to invade, survive and continue their lifecycle inside the host. The malarial parasite that infects humans specifically targets the human red blood cells. In the red blood cells, it consumes hemoglobin in order to survive and reproduce.

Dr. Sharma and his collaborators have been looking at the mechanisms by which the parasite makes its own proteins for survival. Using this knowledge they have been attempting to produce inhibitors that will block protein synthesis in the parasite. The inhibitors would prevent the parasite from making the proteins thus making its survival in the host impossible. The team has been looking specifically at 36 enzymes from a family that helps the malarial parasite produce proteins for survival. Each of these is vital for the parasite's survival. Through these studies, Sharma and his collaborators have been able to validate several compounds based on structural analysis of critical enzyme-drug complexes that would then help develop a generation of drugs that could treat or prevent infection. The major challenge that researchers face is that the parasites continue to evolve and eventually become drug resistant. They are in a continuous race, and any drug developed will need to stay ahead of the organism's ability to evolve and adapt.

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