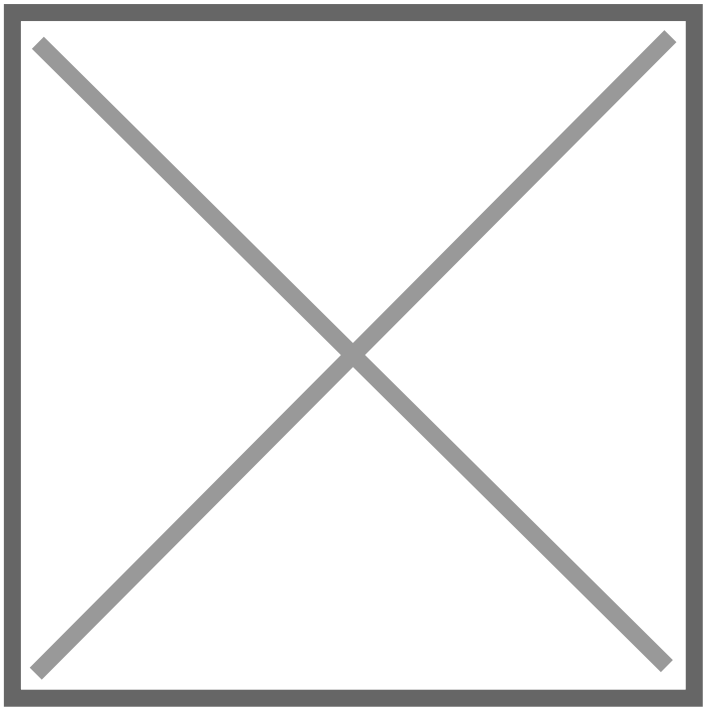
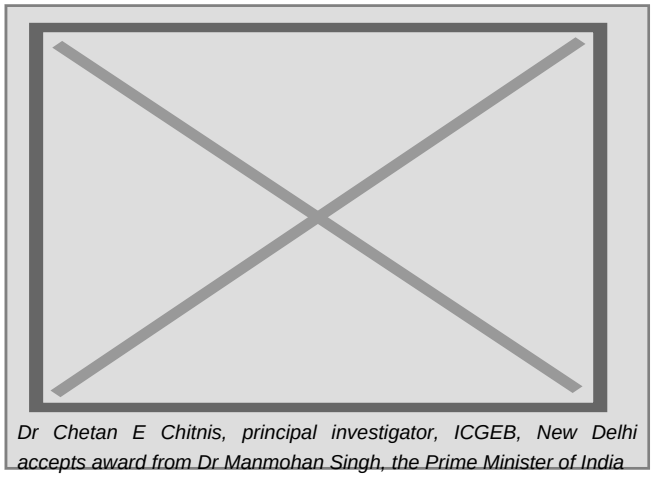
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ICGEB cracks malaria puzzle: Is onto the first viable vaccine

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Dr Chetan E Chitnis, principal investigator at the International Center for Genetic Engineering and Biotechnology (ICGEB) and recipient of the Infosys Award 2010, has cracked the puzzle on understanding the interactions of malarial parasite with its host, leading to the development of the first viable malaria vaccine.



Dr Chetan E Chitnis, principal investigator, ICGEB, New Delhi accepts award from Dr Manmohan Singh, the Prime Minister of India

After years of intensive research, the research group at ICGEB headed by Dr Chitnis cracked the puzzle on processes involved in invasion of malaria parasite in red blood cells (RBCs) thereby streamlining the development of first viable vaccine against malaria.

Dr Chitnis's team is currently working on two vaccines - one for plasmodium falsiparum and the other for plasmodium vivax - both strains are found to be widely prevalent in India. While the vaccine for plasmodium Falsiparum has entered phase I clinical trials, the team is in the process of developing the plasmodium vivax vaccine in large quantities and taking it forward to clinical trials.

Speaking exclusively to BioSpectrum, Dr Chitnis says, Ã¢â?¬Å?Our research tries to understand how the malaria parasite invades red blood cells and thereafter the vaccine will look at blocking that process that in turn blocks the disease.Ã¢â?¬?

If commercialized, these vaccines could be a blessingin disguise for a country like India, whose malaria-afflicted population comprises a share of approximately two-thirds of all confirmed malaria cases in South-East Asia, with five states - Orissa, Chhattisgarh, Madhya Pradesh, Jharkhand and West Bengal Ã¢â?¬â?? accounting for 60 percent of these cases. Other highly-endemic states are Arunachal Pradesh, Assam, Meghalaya and Tripura. Reports indicate that malaria causes 16,000 to 200,000 deaths every year in India alone.

An alumnus from the Indian Institute of Technology, Bombay (IIT-B) with an MSc degree in physics, Dr Chitnis completed his Master of Arts in Physics from Rice University, Houston (post his degree from IIT-B) and PhD in biophysics from the University of California, Berkeley. He was a visiting fellow at the National Institutes of Health, Bethesda and joined ICGEB as a staff research scientist. He is currently a principal investigator with the Malaria Research Group. An international research scholar of Howard Hughes Medical Institute, US and a senior research fellow of the Wellcome Trust, UK, Dr Chitnis was recently awarded with the Infosys Prize 2010 by the Indian Prime Minister, Dr Manmohan Singh, for his pioneering work in understanding the interactions of the malarial parasite and its host, leading to the development of a viable malaria vaccine.

Genesis

It was Dr Chitnis' stint at the National Institutes of Health (NIH), US, as a post-doctorate scholar in 1991, that led him to begin his research activities in malaria. He joined a research group headed by Dr Louis H Miller. Dr Miller and his team made a breakthrough with the discovery that a malaria parasite (plasmodium vivax), in order to invade the RBCs, binds itself to a protein on the RBC called the duffy protein. The binding process between the parasite and the host takes place through a protein on the former called the duffy-binding protein. Dr Chitnis then decided to pursue his research work on diseases relevant to developing nations.

Dr Miller also discovered that those who had duffy positive were more vulnerable to contracting malaria as against those who are duffy negative. Ã¢â?¬Å?In Africa, most of the people are duffy negative, hence, the malaria incidence is low. In India, most of us are duffy positive hence we are more prone to malaria,Ã¢â?¬? adds Chitnis.

At NIH, Dr Chitnis primarily looked at identifying the binding region of duffy-binding protein and making antibodies to block further invasion. Ã¢â?¬Å?We wanted to know which part of the duffy-binding protein to target and what part of the protein is actually involved in that binding interaction,Ã¢â?¬? he adds. At that time, the duffy-binding protein was huge in size measuring up to 150 kilo daltons. The team then narrowed it down to 40 kilo daltons.

Vaccine Initiatives

Subsequently, Dr Chitnis moved back to India and continued his research work. After setting-up his lab at ICGEB, Dr Chitnis further narrowed down the duffy-binding region and also identified the amino acids that were involved in the binding process. Ã¢â?¬Å?We did a lot of structure function studies on the binding domain,Ã¢â?¬? adds Dr Chitnis. The team hence identified the exact binding pocket. Ã¢â?¬Å?These processes are important because vaccines for malaria parasites is difficult to make due to its variations. If you make a vaccine for one it will not work for another parasite,Ã¢â?¬? he adds.

These processes were instrumental in the development of the malaria vaccines. Dr Chitnis and team has also developed another vaccine for plasmodium Falsiparum by identifying erythrocyte-binding protein on malarial parasite that binds to the host RBC. This has been a parallel development along with the plasmodium vivax vaccine. Development of the plasmodium falsiparum vaccine was divided into two components. One component-based research work has been conducted by ICGEB's director, Dr Virendra Chauhan and his team, the other component has been developed by Dr Chitnis and team. Subsequently, they mixed the two components and developed the vaccine on the same rationale of antibodies blocking invasion of the parasite and those methods have been transferred to Hyderabad-based Bharat Biotech. Ã¢â?¬Å?Vaccine was produced, which then went into toxicology studies and entered phase I clinical trials in Bangalore. The vivax vaccine will also follow the same route,Ã¢â?¬? says Dr Chitnis.

In terms of infrastructure, Dr Chitnis established a pilot recombinant protein production facility at ICGEB that has been used to develop methods to produce recombinant protein-based malaria vaccines. A legal entity called the Malaria Vaccine Development Program (MVDP), established by ICGEB and funded by the Bill and Melinda Gates Foundation, is looking at the the translational work of this endeavor. Ã¢â?¬Å?We want to expand our activities on malaria vaccines and take more leads to clinical trials to achieve that you need an entity to manage the translational work. It is more like a small biotech company,Ã¢â?¬? adds Dr Chitnis.

Future

Dr Chitnis is determined to focus his efforts on malaria research. He reveals that there are some avenues opening up in his lab wherein his team is looking at basic problems in invasion of malaria parasite. This opens up vistas in drug development.

For the duffy-binding protein, Dr Chitnis' team has identified molecules that help in invasion and subsequently identify signals that trigger secretion/release to the surface. That has opened up a new field of signaling mechanisms during invasion. And that in turn opens up avenues for drug development.

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