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On quest for malaria remedy

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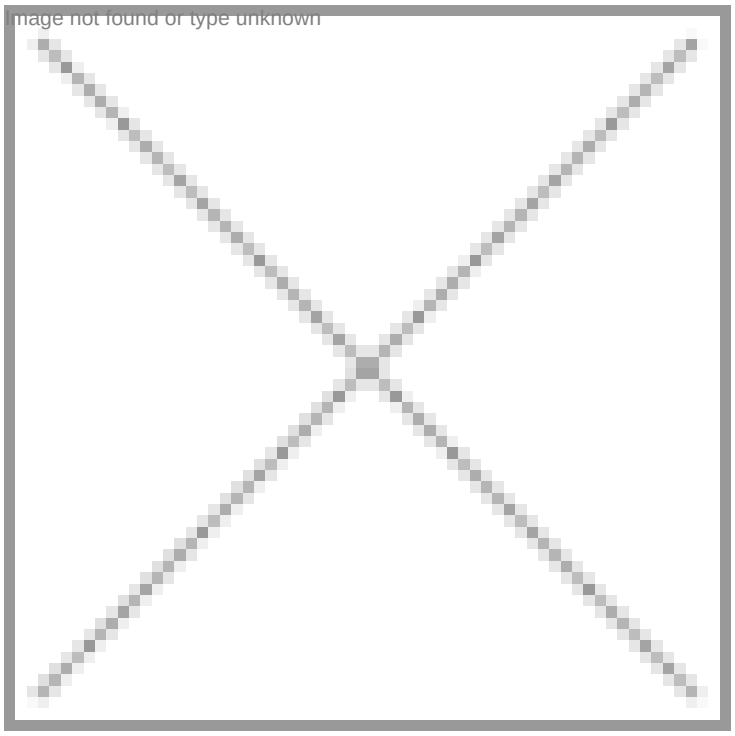

BioSpectrum Person of the Year Award 2011

Ignoring greener pastures abroad, they returned home to steer the efforts in malaria vaccine research and development. For both Dr Virander Singh Chauhan (R) and Dr Chetan E Chitnis (L), science is not just a livelihood, it is a huge responsibility towards society.

With their breakthrough research on the malarial parasite, Dr V S Chauhan, director, International Center for Genetic Engineering and Biotechnology (ICGEB), New Delhi, and Dr Chetan Chitnis, principal investigator, malarial group, ICGEB, have brought India one step closer to the dream of having a vaccine for malaria.

Their decade-long work led to the development of a first generation vaccine, MJAIVAC1, which is based on combination of two merozoite antigens (MSP-119 and EBA-175). The vaccine is presently being tested for safety and immunogenicity in a phase I clinical trial, the first for a malaria vaccine developed in India. The ICGEB has also developed a portfolio of novel antigens that is currently at different stages of pre-clinical development. Also, the center has developed a vaccine, PvDBPII, for Plasmodium vivax and it is being produced by a biotechnology company for a phase I trial. The

ICGEB program has been largely funded by the Department of Biotechnology (DBT), the Bill & Melinda Gates Foundation, Malaria Vaccine Initiative and the European Vaccine Initiative.

Taking malaria head-on

Dr V S Chauhan, who joined the ICGEB in 1988, chose to take the less trodden path. He looked at the blood stage of the parasite and cultured it in the lab. He studied Plasmodium falciparum free merozoites and infected red blood cells (RBCs) that distinctly affect soluble CD40 ligand-mediated maturation of immature monocyte-derived dendritic cells. Dr Chauhan also put his efforts into identification and characterization of a novel Plasmodium falciparum merozoite apical protein, involved in erythrocyte binding and invasion. In his own words, he had â€œnightmares about how to go forward during this challenging taskâ€?.

His malaria group at the ICGEB developed procedures to prepare recombinant vaccine target antigens and the vaccine formulation was developed with industrial partners for clinical trials in India. His work on understanding the mechanism of action of antimalarial drugs, such as chloroquine and artemisinin, led to the development of high throughput screens for malaria drug discovery.

Dr Chetan Chitnis joined the ICGEB in 1996 with expertise in the area of host pathogen interaction. Before this, he had worked as a post-doctorate scholar in a research group headed by Dr Louis

"I have known Dr VS Chauhan for more than two decades. I always felt that he personifies the term 'leading from the front' because under his exceptional scientific caliber and vision, the ICGEB has transcended into a center with emphasis on innovative and path breaking research. I had the opportunity of visiting Dr Chetan Chitnis' Laboratory of Parasitic Diseases at the NIH, US, in 1993. He came across as a trailblazer with a passion for serious research"

Dr T S Rao
Adviser, DBT, Ministry of Science and Technology, Government of India

H Miller at the National Institutes of Health (NIH), US. The work helped him understand that the binding process between the parasite and the host takes place through a protein on the former, called the duffy-binding protein. Subsequently, Dr Chitnis returned to India and continued his research and his experience helped him look at identifying the binding region of duffy-binding protein and making antibodies to block further invasion.

After setting-up his lab at the ICGEB, Dr Chitnis further narrowed down the duffy-binding region and identified the amino acids involved in the binding process. â€œWe did a lot of structure functional studies on the binding domain,â€? adds Dr Chitnis. His team identified the exact binding pocket. â€œThese processes are important because vaccine 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,â€? he adds.

"A very good example of team work, combined with innovative research embedded in excellent basic science"

Dr S Natesh
senior advisor (scientist-H), DBT, Ministry of Science & Technology, Govt. of India

The team at IGCEB, led by Dr Chauhan and Dr Chitnis as the principal investigator, chose to work on more difficult but potential areas. Efforts were directed at building the rationale for blood stage malaria vaccine candidates based on Plasmodium falciparum and Plasmodium vivax proteins that mediate erythrocyte invasion.

Dr Chitnis and the team also developed another vaccine for plasmodium falciparum by identifying erythrocyte-binding protein on malarial parasite that binds to the host red blood cells (RBC).

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The development of vaccine for Plasmodium falciparum was divided into two components. One component-based research on merozoite antigens was conducted by Dr Chauhan and his team, while the other component was developed by Dr Chitnis and the team. They mixed the two components and developed the vaccine on the same rationale that antibodies block invasion of the parasite. The methods have been transferred to Hyderabad-based Bharat Biotech.

"Drs Vijender Chauhan and Dr Chetan Chitnis are two highly accomplished malaria researchers who have jointly developed India's first indigenous malaria vaccine that is currently in phase I clinical trials in India. Translational research is an extremely challenging task and their successful efforts have placed India as a strong player globally in malaria vaccine development. They both continue to lead high quality malaria research programs and their achievements deserve many congratulations and appreciation"

Dr Deepak Gaur
principal investigator, Malaria Group, ICGEB

Dr Chauhan, who dedicates the success to the young members of the team, says it is teamwork that has brought them so far. Appreciating him for the freedom he has given to the researchers, Dr Chitnis says, â€œthe ICGEB gives the freedom to do things. There is no bureaucratic set-up here and Dr Chauhan has provided us all the liberty to do things.â€?

Both Dr V S Chauhan and Dr Chetan Chitnis remain skeptical about the breakthrough achieved because of the adaptability and mutability of the pathogen involved. â€œWe are at the verge of getting somewhere but can't say that we are fully sure. Breakthrough in my understanding may work or may not,â€? says Dr Chitnis. â€œAny breakthrough is welcome, after years of hard work. But these are long processes that include the phase I and II and the final field trials.â€?

Eyes set on challenges

The people who are duffy positive are more vulnerable to malaria as against those who are duffy negative. â€œIn Africa, most of the people are duffy negative, hence, malaria incidence is low. In India, most of us are duffy positive, hence we are more prone to malaria,â€? says Dr Chitnis.

Dr Chauhan adds that vaccines can't be the final solution and drug development needs attention. Raising an important issue of possible artemisnin resistance, he says, â€œThere have been reports of resistance in Cambodia, Thailand and if it reaches Burma and the Northeastern part of India, then things can get very messy.â€?

"Both of them richly deserve the Biospectrum Award, 2011. They have carried out pioneering studies with the malarial parasite, both in terms of understanding the basic biology and applying the knowledge to contain this disease. They are the only group in the country to have embarked on developing vaccines against falciparum and vivax malaria, which has been an international challenge for decades. This is a unique effort in global terms and is recognized as such"

Dr G Padmanaban
National Academy of Sciences, India (NASI)-platinum jubilee chair/ hon professor, Indian Institute of Science, Bangalore

â€œI am worried about the fact that there is no drug available for hepatitis C, dengue, chikungunia and there is also a fear of drug resistance. We need to do something about it immediately as Artemisnin should be used only with a drug but it slows down the process. Both with tuberculosis and malaria, we are near the end of the road. We have to start working on it right now and keep investing heavily,â€? adds Dr Chauhan.

Both Dr Chauhan and Dr Chitnis agree that quality papers are being published and researchers are doing good work in India. However,

research in India has so far not been translated into products. Citing the lack of a skilled workforce for translation in the academia, he says collaborations with the industry is important. â€œThe basic research of academia and translation expertise of industry, combined together will definitely give more results,â€? says Dr Chauhan.

Dr Chitnis doesn't consider the comparison of Indian enterprises with the West to be fair. Giving an example, he says, â€œWhen I was at the NIH, the annual budget wa 1,56,000 crore ($30 billion), which is much more than the total funding of the agencies here put together.â€?

Agreeing with him, Dr Chauhan says, â€œI think we don't have enough manpower. Government support is great and, being part of government committees, I understand how much the government is doing. The government-funded conferences were unthinkable a few years ago, but it is happening now.â€?

Different roles, one goal

Dr Virander S Chauhan, director, ICGEB, New Delhi

Brought up in a middle-class family, Dr Virander S Chauhan struggled hard to study with little guidance from parents and relatives. Being the topper of his school earned him a National Talent Scholarship that played an important role in his life.

Dr Chauhan, whose dream job was to be a teacher, joined St Stephens College as a lecturer after completing his masters' degree. He simultaneously worked on his PhD in chemistry at Delhi University and finished it in 1974. He received the Rhodes Scholarship and went to Oxford University, where he finished his D Phil in 1977.

He came back to India in 1979 and chose to teach at IIT Kanpur, where he continued until 1981. He continued with his research at the University of Delhi and joined the International Center for Genetic Engineering and Biotechnology (ICGEB) in 1988 and headed the malaria research group.

In 1998, he became the second director of the ICGEB but continued to lead the malaria research group.

Dr Chauhan is also well-known for his work in the area of design, synthesis and utility of conformationally defined peptides and is the founder president of the Indian Peptide Society. He has published many papers and encouraged many well-known scientists to carry forward their research.

Very fond of running at a younger age, Dr Chauhan now spends his free time listening to Indian classical music and reading.

Dr Chetan Chitnis, principal investigator-Malaria Research Group, ICGEB, New Delhi

Dr Chetan Chitnis comes from a family of scientists. While his father is an astrophysist, his mother is a biochemist. He spent his childhood in an environment where science was always a subject of discussion. â€œHowever, it took some time for me to actually figure out my interest. I did my integrated MSc course in physics from IIT Bombay,â€? says Dr Chitnis.

Dr Chitnis received his PhD in biophysics from the University of California, Berkeley, and did postdoctoral research on malaria in the Laboratory of Parasitic Diseases at the National Institutes of Health, Bethesda. He was instrumental in starting the Malaria Vaccine Development Program, a joint venture between the DBT, PATH and the ICGEB.

He has authored more than 70 research papers and has received many awards, including the Infosys Prize for Life Sciences, Shanti Swaroop Bhatnagar Prize for Medical Sciences, Wellcome Trust Senior Research Fellowship, Howard Hughes International Research Scholarship, and M O T Iyengar Award for Research in Malaria from the Indian Council of Medical Research.

Being a dedicated researcher, Dr Chitnis believes that for a scientist, the real thrill is not in getting the awards but actually doing quality of research he does. He considers himself as fortunate to have the good mentor like Dr Liu Miller, who guided him at the NIH. A family man, Dr Chitnis spends most of his free time in the company of his children. He is a voracious reader and also enjoys hiking.

Hopes for the future

According to Dr Chauhan, India is coming up as the hub of vaccines. â€œThere are many vaccine factories. Half of Africa has been immunized with the vaccines produced in India. If we stay focused, the day is not far when we will be the

leaders.â€?

"Prof Chauhan has the special ability to make things happen. The malaria vaccine efforts of Prof Chauhan and Dr Chitnis has brought international visibility to Indian Science"

Dr Navin Khanna
group leader, mammalian biology, recombinant gene products, ICGEB

Dr Chitnis is determined to focus his efforts on malarial research. For the duffy-binding protein, the team has identified molecules that help in invasion and subsequently identified signals that trigger secretion or release to the surface. This has opened up a new field of signaling mechanisms during invasion. And that, in turn, has opened up avenues of drug development.

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The phase I trial for falciparum vaccine is on and results are expected by March 2012. â€œIf the results are positive, then we will proceed to phase II. If the results are not satisfactory, we will have to go back and do modifications,â€? says Dr Chauhan. â€œIt is difficult to predict when will the actual product development happen, but if the things go on smoothly, then possibly we may have the drug by the next 10 years.â€?

Dr Chauhan says his focus has been to do things well. â€œWe are keen on technology development and have transferred dengue detection kit and hepatitis C vaccine to the industry. We never give exclusive license as non-exclusiveness will help us to disseminate the technology. We may not make profit but we are not here to make money,â€? he says.

-**Rahul Koul** in New Delhi