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NEWS & VIEWS

Issue 28 | February 2023

International Day of Women & Girls in Science

11th February

INTERVIEWS

Professor Ashis Kumar Das,
Department of Biological Sciences,
BITS Pilani, Rajasthan

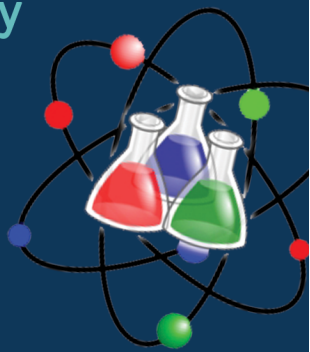
Dr Nivedita Gupta,
Scientist F & Head, ECD division,
ICMR headquarters, New Delhi

UPCOMING EVENT

Lecture Series on Infectious Diseases 2.0, Lecture 02 by **Prof (Dr) Mitali Chatterjee,** IPGMER, Kolkata

National Science Day

28th February



EDITORIAL | INTERVIEWS | RESEARCH IN SPOTLIGHT
NIMR & MERA-INDIA ACTIVITIES | MALARIA THROUGH THE LENS OF RESEARCHERS | UPCOMING EVENT

Editorial

Dear Readers,

MERA-India team brings you the twenty-eighth issue of our newsletter, “News & Views’.

The month of February marks two of the significant days observed across the world and India: the International Day of Women and Girls in Science (11th February), and the National Science Day (28th February). Adopting a scientific approach and thinking are the hallmarks of a progressive and healthy society. While the applications of science and technology in our routine life are plenty, we take this moment to remember and acknowledge all the great scientists who were behind the innovations and discoveries which led to advancements in the field of medicine and health resulting in the saving of countless lives. MERA-India is committed to provide a platform to connect and support scientists and young researchers, not only in terms of funding to execute the research ideas but also through facilitating interactions and guidance with experts in the field.

In January 2023, we organized lectures from two eminent Indian scientists, the highlights of which are presented in this issue. The opening lecture of the ICMR-NIMR & MERA-India Lecture Series on Infectious Diseases 2.0 was delivered by Dr Radha Rangarajan {Director, CSIR-Central Drug Research Institute (CDRI)}. Dr Madhumita Dobe, (Former Dean, Director-Professor and Head of the Department of Health Promotion and Education, All India Institute of Hygiene & Public Health) gave a lecture in the ICMR-NIMR & MERA-India Distinguished Lecture series.

In the “Malaria Scientists to Watch” section, we have covered inspirational and enlightening interviews of Professor Ashis Kumar Das (Birla Institute of Technology and Science-Pilani) and Dr Nivedita Gupta (Scientist F and Head, Epidemiology and Communicable Diseases Division, ICMR). In the “Research in Spotlight” section, we have highlighted three recent studies describing a molecular and web-based tool to identify imported *Plasmodium vivax* malaria cases by Trimarsanto H. *et al*; a new WHO glass bottle bioassay method standardized and validated by Corbel V. *et al*. for assessing the sensitivity of mosquitoes to insecticides; and impact of insecticide resistance on the vector competency by Suh PF. *et al*.

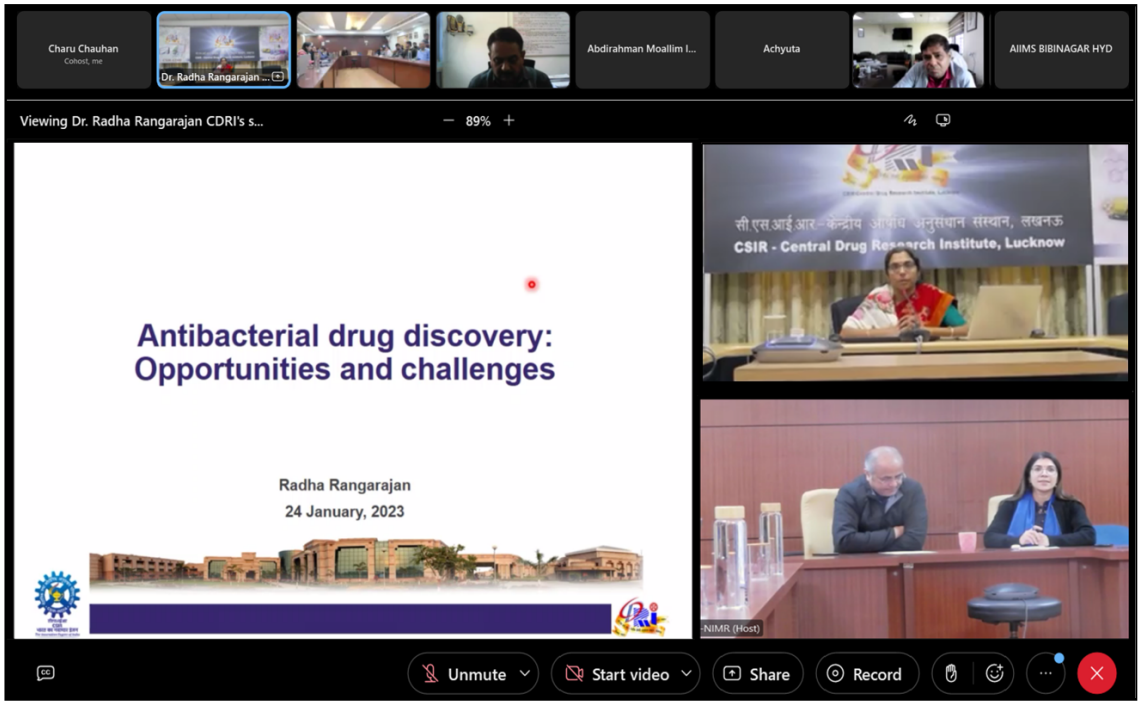
In the section “Malaria Through the Lens of Researchers”, we have featured one of the shortlisted entries of the MERA-India Image Competition 2022, submitted by Ms Pooja Rohilla, a PhD student at the National Institute of Malaria Research (NIMR), Delhi. In the “Upcoming Event” section, we have provided details of the second lecture of the Lecture Series on Infectious Diseases 2.0, to be delivered by Prof (Dr) Mitali Chatterjee {professor and head of the department of pharmacology, the Institute of Post Graduate Medical Education & Research (IPGMER)}.

We hope that you will find this issue engaging and fascinating. Please write to us for any feedback or suggestions regarding the newsletter’s content at meranewsletter@gmail.com.

With best wishes,
MERA-India team

ICMR-NIMR & MERA-India Activities

Launch of Lecture Series on Infectious Diseases 2.0: Lecture 01 by Dr Radha Rangarajan



After the successful culmination of the ICMR-NIMR & MERA-India first Lecture Series on Infectious Diseases last year with twelve talks from renowned scientists around the world on topics ranging from malaria, COVID-19, tuberculosis, visceral leishmaniasis, and fungal infections, etc., the Lecture Series on Infectious Diseases 2.0 was launched last month in January 2023. The opening lecture of the series was delivered by Dr Radha Rangarajan, Director, CSIR-CDRI, Lucknow, India. The core research interests of Dr Rangarajan are in understanding the mechanisms of antimicrobial resistance and developing novel approaches to disabling resistant pathogens. Dr Manju Rahi (Director in-charge, ICMR-NIMR) welcomed Dr Rangarajan and Dr Sachin Sharma (Chief Consultant, MERA-India) briefly introduced the speaker to the audience.

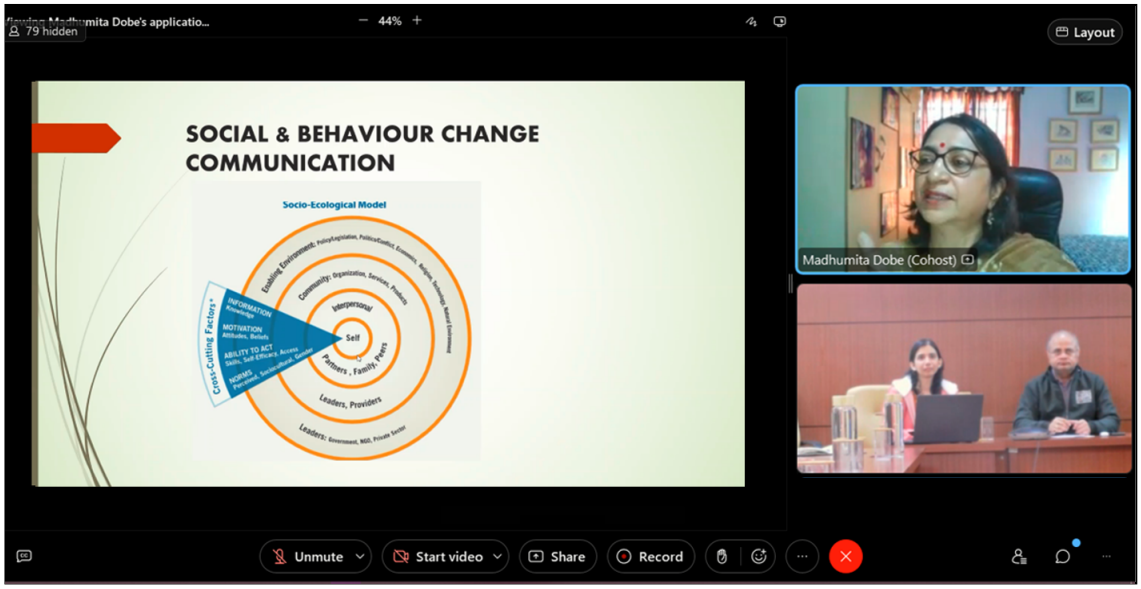
Dr Rangarajan talked on the topic of “Antibacterial drug discovery: opportunities and challenges” and highlighted the threat of antimicrobial drug resistance which could lead to 10 million deaths annually by the year 2050. She narrated the history of antibiotics development and described the challenges, including the inevitable emergence of resistance in all antibiotics - the time course of which is quite difficult to predict and thus stressed the need for constant research to develop new drugs. With examples, she illustrated the use of artificial intelligence and machine learning to overcome the challenges

in antibacterial compound identification, which could help save time and cost to introduce new compounds from the research lab to the clinic. She also discussed the possible ways to encourage the engagement of the pharmaceutical sector in antibiotic development,

including the use of technology for accelerated candidate drug selection and quicker regulatory approvals. Dr Rangarajan concluded by calling upon the various sectors, including clinical, academic, research, and commercial, to work collaboratively for constructing a robust antibacterial drug pipeline.

Following the lecture, Dr Rangarajan answered the questions from the attendees. The session was concluded by Dr Sharma with a vote of thanks to the speaker and all the attendees.

Distinguished Lecture by Dr Madhumita Dobe



The distinguished lecture was delivered by Dr Madhumita Dobe on 30th January 2023, she is the former Dean and Director - Professor (Public Health) and Former HOD, of the Department of Health Promotion & Education at All India Institute of Hygiene & Public Health, Kolkata (Ministry of Health & Family Welfare, Government of India). At present, she is the Chairperson of FAITH (Foundation for Actions and Innovations towards Health Promotion). Dr Sachin Sharma welcomed Dr Dobe and introduced her to the audience.

Dr Dobe delivered an illuminating lecture entitled "Learning from failures for future successes - changing community behavior". She illustrated the learnings from prior work in the field of community behavior and indicated that until now community behavior has been seen through the lenses of KAP (Knowledge, Attitude, and Practice), but only knowledge is insufficient to bring about behavior changes. People may or may not change their behavior based on knowledge or perceptions due to psychological defense mechanisms called cognitive dissonance. Further, she highlighted that all interventions towards elimination are focused on knowledge, assuming that increasing knowledge will help in an attitudinal change leading to behavioral change. Dr Dobe suggested that people should look beyond KAP. People live in communities and hence culture has an influence on health, it affects the perceptions of health, illness, and death, beliefs about the causes of diseases, and how illnesses are experienced and expressed. She explained evidence-based, theory-based, and system-based approaches to find what is lacking and what needs to be done for

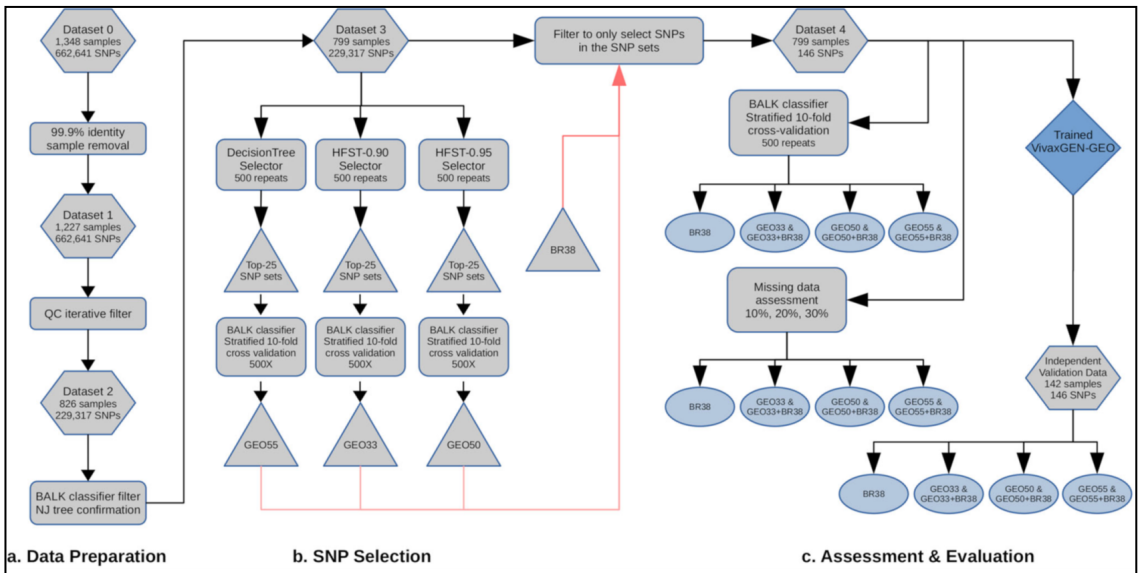
changing community behavior. She suggested a P process, to plan any intervention, which include components like analysis, strategic design, development and testing, implementation and monitoring, and evaluation and planning. In the end, Dr Dobe highlighted various research gaps, which can be pursued by the researchers.

After the lecture, Dr Dobe addressed all the queries of the audience. The session concluded with Dr Sharma thanking the speaker and the attendees.

The recording of this lecture is available on the MERA-India website (https://www.meraindia.org.in/lecture-series).

Research in Spotlight

Trimarsanto H. *et al*., *Commun Biol*. 2022: A molecular barcode and web-based data analysis tool to identify imported *Plasmodium vivax* malaria

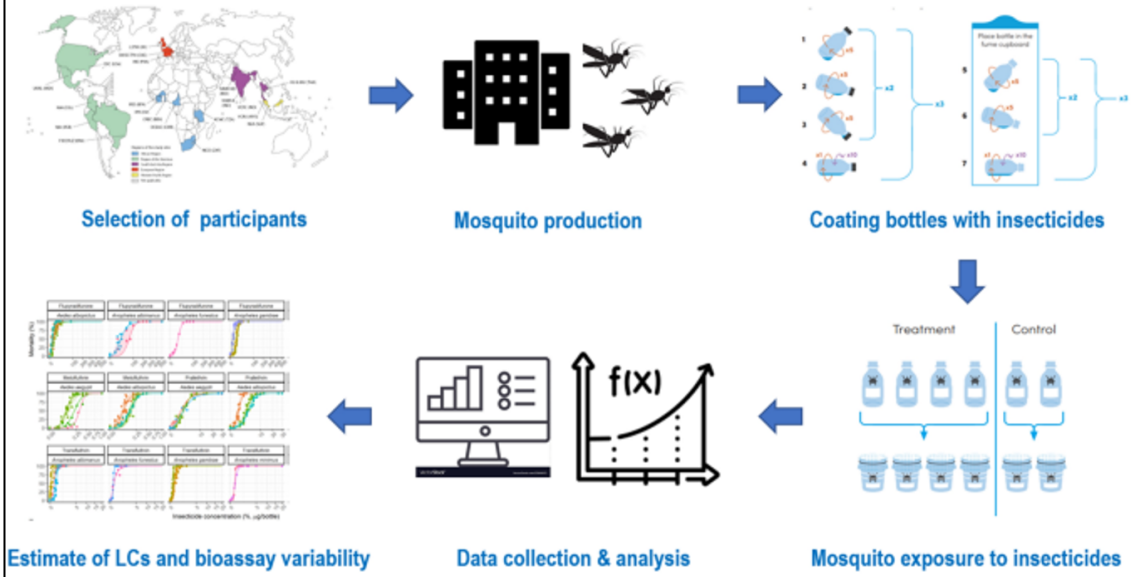


Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9789135/

The tracing of patient travel history has been traditionally used to classify malaria infection as local or imported. However, in patients carrying dormant *Plasmodium vivax* hypnozoites, which could reactivate weeks to months after the initial infection, this correlation does not work. Molecular approaches can be exploited to trace the history and origin of infections in such cases. In this study, the authors have analyzed 799 *P. vivax* genomes from 21 countries, with representations from all major *P. vivax* endemic countries, and applied machine learning approaches to map the country of the infection origin. The authors have

reported three new SNP panels (GEO barcodes), which have a high predictive capacity to map the infection originating from the representative countries. The authors have further developed a likelihood classifier integrated with the open-access platform (http://geo.vivaxgen.org) for ready analysis and interpretation of the barcoding sequencing data for users with limited or no bioinformatics or genetics expertise. This would thus help the malaria control programs to strengthen surveillance and plan appropriate malaria control and management strategies upon the detection of a positive case originating from a particular region.

Corbel V. *et al., Parasit Vectors. 2023*: A new WHO bottle bioassay method to assess the susceptibility of mosquito vectors to public health insecticides: results from a WHO-coordinated multi-centre study



Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9863080/

The surveillance and monitoring of mosquitoes' resistance to insecticides are done using the WHO test tube assay method in which the mosquitoes are exposed to insecticide-impregnated filter papers. However, the efficacy of some of the new insecticides using the test tube assay could not be determined because of the instability of the insecticides on the filter paper. This multi-centric study describes the development and validation of a newly developed WHO glass bottle bioassay method, as an alternative to the WHO test tube assay method, for assessing the susceptibility of mosquitoes to the available and newly developed insecticides. In this study, 21 internationally recognized laboratories located worldwide assessed the susceptibility of about 2,00,000 mosquitoes, including five *Anopheles* spp. (*Anopheles albimanus*, *Anopheles gambiae sensu stricto*, *Anopheles funestus sensu stricto*, *Anopheles minimus sensu stricto*, and *Anopheles stephensi*) and two *Aedes* spp. (*Aedes aegypti*, *Aedes albopictus*), to seven insecticides, with five different modes of action, using the WHO glass bottle assay method. The selected insecticides were

unstable after impregnation on the filter papers. For each of the insecticide–species combinations, the concentration-response curves were plotted to determine the LC50 and LC99 (insecticide concentration killing 50% and 99% of the test population) as well as OI50 and OI99 (insecticide concentration inhibiting oviposition of the test population by 50% and 99%). The study has produced the largest dataset ever for mosquito susceptibility. The bioassay variability in terms of mortality and oviposition inhibition was also compared across the participating laboratories and was <10% for most of the combinations of mosquito species and insecticides. This new assay method can thus be adopted to screen the mosquitoes for susceptibility to new insecticides which are not stable on the filter papers but have the potential to be used for effective vector control.

Suh PF. *et al., Malar J.* 2023: Impact of insecticide resistance on malaria vector competence: a literature review

Table 2 Summary of studies assessing the impact of insecticide resistance on the longevity of malaria vectors

Study species	Origin of strains	Class of insecticides	Resistance mechanism(s)	Pre-Exposure[a]/Exposure[b] to insecticide	Effect on longevity	References
An. gambiae s.l	Field	PY	Not available	Deltamethrin and permethrin[a]	RR longevity > SS longevity	[97]
	Field	PY & OC	*kdr*	Not applied	RR longevity < SS longevity	[96]
	Field	PY	Not available	Permethrin (Net) [b]	RR^{e} longevity = RR^{ne}	[98]
	Laboratory	PY & OC	*kdr* & P450	Permethrin (Hut-net) [b]		
	Laboratory	PY	Not available	Deltamethrin[b]	RR longevity < SS longevity	[99]
	Laboratory	PY	kdr, P450 and esterase	Not applied	RR longevity > SS longevity	[100]
	Laboratory	OC	*kdr*	DDT[a]	RR longevity = SS longevity	[33]
		CA	*ace*-1	Bendiocarb[a]	RR longevity > SS longevity	
	Laboratory	OC	*kdr*, *GSTe*, P450 & Es	Not applied	RR longevity = SS longevity	[101]
	Laboratory	OC	*GSTe*, P450 & Es	Not applied	RR^{b} longevity > RR^{s}	[102]
	Laboratory	OC	*GSTe*, P450, Es;*kdr*	Not applied	RR longevity < SS longevity	[103]
				DDT[a]	RR^{e} longevity = RR^{ne}	
				Permethrin[a],	RR^{e} longevity < RR^{ne}	
				Deltamethrin[a]	RR^{e} longevity < RR^{ne}	
				Malathion	RR^{e} longevity < RR^{ne}	
An. funestus	Field	OC	*GSTe2*	Permethrin (Net) [b]	RR longevity > SS longevity	[104]
	Field	PY & OC	*GSTe2*	Not applied	RR longevity > SS longevity	[105]
	Laboratory	PY	Not available	Not applied	RR longevity > SS longevity	[106]
	Laboratory	PY & CA	*P450-a*	Not applied	RR longevity = SS longevity	[107]
	Laboratory	PY & CA	*P450-a*	Not applied	RR longevity = SS longevity	[108]
			P450-b		RR longevity = SS longevity	
			P450-a/P450-b		RR longevity = SS longevity	

PY: Pyrethroid; OC: Organochlorine; CA: Carbamate; GSTe: Glutathion S-transferase; Es: Esterase; *kdr*: Knock down resistance; P450: Cytochrome P450 monoxygenase; RR: resistant strain, SS: susceptible strain; RR^{e}: resistant strain exposed to insecticide; RR^{ne}: resistant strain non-exposed to insecticide; RR^{b}: Resistant strain fed on blood; RR^{s}: Resistant strain fed on sugar; > more; < less; = equal

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9847052/

Insecticide resistance is one of the major roadblocks for achieving the goal of malaria elimination. The insecticide resistance in Anopheline mosquitoes was reported for the first time in the 1950s, and since then it has spread to most sub-Saharan African malaria-endemic countries and jeopardizing the efforts of vector control and disease management. Various studies showed the presence of resistance in different states of India as well.

Insecticide resistance in mosquitoes can be achieved through the following mechanisms, (1) metabolic resistance: degradation of insecticide molecules by detoxification enzymes, (2) target site resistance: modification of the target affinity of the insecticide, (3) cuticular resistance: reduced penetration of the insecticide and, (4) behavioral resistance: avoidance of insecticide-treated surfaces. To find out the effect of these intrinsic changes on vector competency, the authors have summarized the published insecticide resistance data showing direct or indirect relation to vector competency including anti-*Plasmodium* immunity, intestinal commensal microbiota, sialome composition, and mosquito longevity. The authors have found that there is not enough data related to the vector competency in relation to immunity and microbiota of the insecticide resistance mosquitoes to conclude their epidemiological importance over the susceptible ones. The authors stated that *Plasmodium* infectivity may increase in the susceptible mosquito due to changes in the expression of blood meal related/immunity genes and microbiota composition. They also found that the longevity of mosquitoes is not affected by the resistance mechanisms. The authors have suggested for further refined research using omics technology for determining the effects of insecticide resistance on vector competency.

Malaria Scientists to Watch

An interview with Professor Ashis Kumar Das

Professor Ashis K Das
Department of Biological Sciences,
Birla Institute of Technology and Science-Pilani,
Rajasthan, India

1. What motivated you to work in the field of malaria research?

I have always been fascinated by the incredible plasticity of an unicellular eukaryotic organism which has adapted to a parasitic existence in two very different environments (mosquito and vertebrate host) to enable the completion of its life cycle. More importantly, I have been primarily interested in the species of this parasite which affects humans, and much of our work is focused on trying to discover/investigate new molecules which could assist in the creation of procedures to enable the reduction of the havoc which these parasites can cause to humans.

2. What has been your most surprising and unexpected discovery in malaria so far?

Our collaborators and we have reported the phenomenon of *Plasmodium vivax* causing severe disease, similar to *Plasmodium falciparum*, from India, since 2005. One of the focus of my group has remained in trying to investigate the genomic and transcriptomic differences in parasites from patient isolates causing severe or uncomplicated malaria. In this process, we have also created “in-vivo” WGCN networks which have enabled the identification of key molecules (HUB genes), many of which have not been studied at all. We feel that some of these molecules could provide leads to new therapeutic or diagnostic targets for both *P. vivax* and *P. falciparum*. We have also published and are currently studying Natural Antisense Transcripts (NATs) produced from the parasite genomes in uncomplicated and severe disease conditions and are trying to decipher their role in natural infection, with respect to, genome regulation leading to increased parasite survival under different conditions. We have been the first to publish on NATs in *P. vivax* and, to our knowledge, the first to highlight NATs in *P. falciparum* from patient-derived parasite material.

3. India has set up a target of malaria elimination by 2030 and has been seeing a decline in the number of cases and deaths. What challenges do you see for India in achieving this goal?

It is heartening that there appears to be a reduction of recorded infections by major human malaria-causing parasites. However, in my opinion, elimination is a goal, which may not be easily achievable in the time mentioned. We have a diversity of environments both urban and rural, which provide niches for vector and parasite survival. Unless the parasite transmission process is completely disrupted, and there are no reservoirs left for the mosquito vectors to reinitiate the process we will always be at a risk for malaria regardless of how heartening the infection data appears to be. Additionally, there is the phenomenon of parasite drug resistance. We have been fortunate in not seeing artemisinin resistance in the country as yet, however, the vigilance has to be permanently at peak to prevent any future issues. Finally, we should not forget the lessons from history. Malaria in the past has been seen to devastatingly reappear when there has been any mitigation in surveillance, prevention, or research efforts.

4. What is one piece of advice that you would like to give to PhD students and early-career researchers?

Be passionate about the research you are doing, however, try to remain practical and pragmatic for the attainment of your objectives.

5. *You have been associated as a mentor for the MERA-India funded multi-centric project on "low-density malaria infection detection and its transmission potential", and also as a fellow in one of the MERA-India funded projects. What potential do you see in MERA-India to support India's malaria elimination target?*

The projects supported by MERA-India are focused on trying to fund niche areas, which could lead to important advances in our fight against malaria. The objective has been to

support ideas and initiatives which would be important for the overall process of elimination. To take an example of the mentioned project, low density infections, if left undetected or studied would always provide a hidden reservoir to initiate the infection process even when number of active cases have significantly reduced. MERA-India is thus an important initiative to initiate targeted research and discovery directly linked to the proposed elimination of malaria from the country.

An interview with Dr Nivedita Gupta

Dr Nivedita Gupta
Scientist F and Head,
Epidemiology and Communicable Diseases Division,
Indian Council of Medical Research,
New Delhi, India

1. As the Head of the Division of Epidemiology and Infectious Diseases at ICMR headquarters, please share with us the ongoing programmes under this division focussing on malaria research.

The Division of ECD has been undertaking and funding comprehensive research on Malaria treatment, prevention, and control. The research encompasses various facets involving the vector, transmission dynamics, human disease, treatment regimens, epidemiological, operation research, and effect of climate change on Malaria. Several studies have been funded with a focus on understanding the role of different/new vectors in Malaria transmission, factors affecting the disease transmission dynamics, monitoring the emergence of insecticide resistance, and finding newer tools to combat resistance. Our research in the past has also included drug trials of newer treatment regimens in standalone or combination regimens. Other important issues like the spread of Malaria through cross-border migration and the role of climate change i.e. temperature, humidity, and rainfall in the changing dynamics of transmission have also been studied systematically. Moving forward, operational research issues to understand the gaps and demonstrate better intervention models for Malaria elimination is a focus in addition to development of newer tools for elimination and achieving the last mile in the end game strategy.

2. India has set up a target of malaria elimination by 2030 and has been seeing a decline in the number of cases and deaths. What challenges do you see for India in achieving this goal?

The major challenges outlined for Malaria elimination in India have been earlier spelled out as large population and overcrowding, lack of hygiene, migration from low to high endemicity zones, the emergence of insecticide resistance in vectors, newer vectors

involved in disease transmission, change in vector behavior due to various factors including climate change, deforestation, etc. However, I also feel that one of the most important challenges is timely diagnosis. Due to the complex lifecycle of the Malaria parasite, diagnosis sometimes becomes challenging and the sensitivity of a particular test would depend on the stage of the disease. Also, asymptomatic Malaria cases are difficult to detect unless community-based RDT screening programs are implemented. However, the asymptomatic carriers contribute to Malaria transmission. It may also be important to have a robust pipeline of new antimalarial drugs. The upcoming Malaria vaccines must also be trialed and kept in our arsenal for elimination. Moving ahead, it may be valuable to explore the role of host-directed therapies in Malaria control.

3. What challenges do you see for women working in STEM?

Women working in STEM do have some challenges but have immense opportunities as well. The key challenge is to maintain a work-life balance and ensure a good upbringing for your children. Mid-career breaks which sometimes become inevitable, really push you back and force you to hand over some of your very key portfolios to other colleagues just to never get them back after your return. However, women who successfully sail through the difficult early career phase mostly emerge as strong and undeterred professionals, who come across as examples of women empowerment and encourage many other young women to take this career path.

4. What is one piece of advice that you would like to give to early-career researchers?

One should always focus on solution based research and avoid blue sky research. A strong research idea has to be backed by a very thoughtfully designed research plan. The study objectives, implementation plan and outcomes should be very clear right from the beginning. Methodology should be aligned to the objectives and desired outcomes. A badly planned study will always give bad results. I advise that all early career researchers should attend proposal writing and research methodology workshops to learn to write good research proposals.

5. *What significance do you see for MERA-India in achieving India's malaria elimination target?*

MERA-India is a strong and focused research initiative to find solutions related to Malaria elimination in India. MERA-India is a very good example of how research and National elimination programs should work together to drive the programmatic strategies through evidence based research. The symbiotic relationship between research and the program should be seen as a very good example, which should be replicated for all ongoing/proposed elimination programs. This will enable implementation of various public health programs in India with a strong research backing.

Malaria Through the Lens of Researchers

In this issue, we are highlighting one of the shortlisted entries in the MERA-India Image Competition 2022, submitted by Ms Pooja Rohilla, a PhD student of Dr Rajnikant Dixit at ICMR-NIMR, Delhi

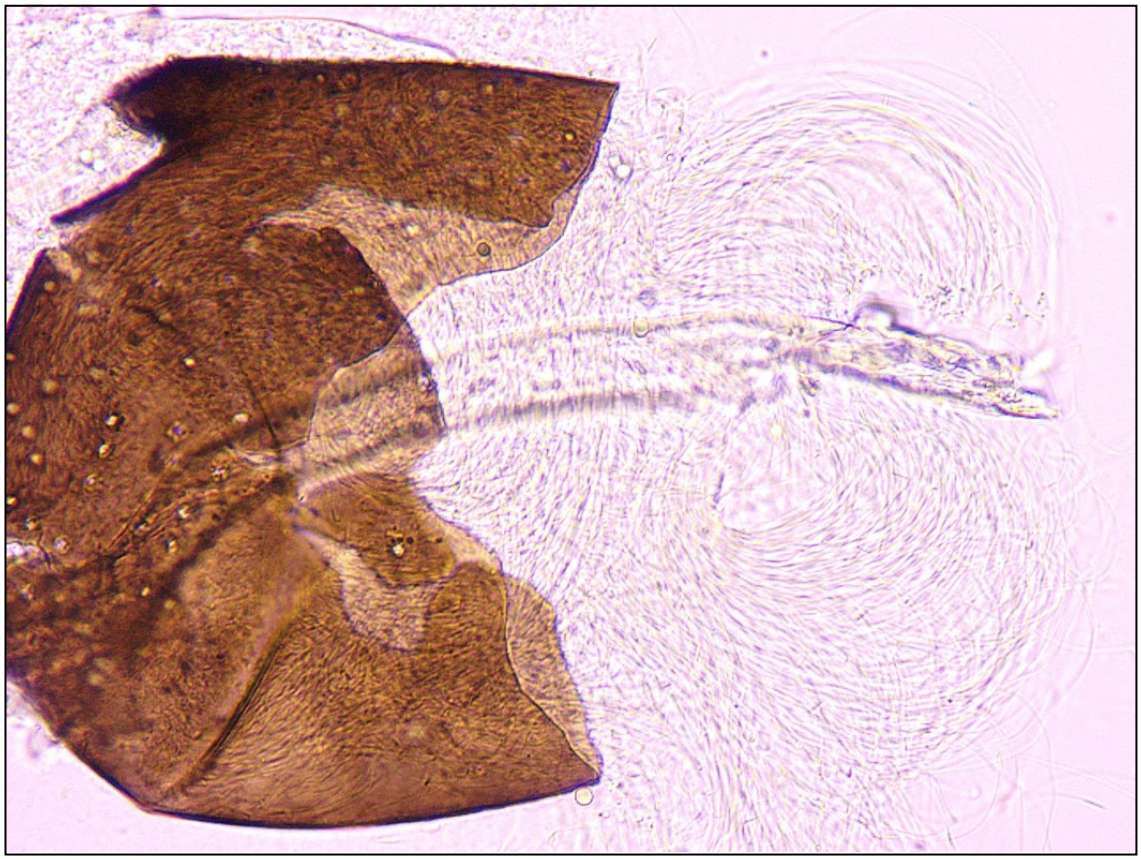


Image title: “Spermatheca of Mated Female of *Anopheles culicifacies*”
A brief description of the image is as follows:
In this image, the spermatheca of a mated female *Anopheles culicifacies* is shown as visualized under the microscope (40X). In females, spermatheca present in the last abdominal segment is a small sac-like structure that stores sperm. In virgin females, it is flattened and seen clear (no sperms) under the microscope, but in the case of mated females, the spermatheca is stretched and sperms were observed. This image shows a ruptured mated female spermatheca (brown colored) so that sperms, having long tails, can be clearly seen coming out of it.

Upcoming Event

Lecture Series on Infectious Diseases 2.0: Lecture 02 by Dr Mitali Chatterjee

ICMR-NIMR and MERA-India are hosting the second lecture in the series "Lecture Series on Infectious Diseases 2.0". Prof (Dr) Mitali Chatterjee, professor and head of the department of pharmacology, IPGMER, Kolkata, will be the second speaker of the series. She has been honored with eminent awards like J. Ammal (Senior Category) Women Bioscientist Award, by DBT, Dr. PN Chhuttani oration, by National Academy of Medical Sciences, Kshanika oration by ICMR, and many more.

Dr Chatterjee will deliver the lecture entitled "Post Kala-azar Dermal Leishmaniasis: a neglected tropical disease that must not remain neglected". She will focus her talk on the last mile challenges faced by the ongoing kala-azar elimination programme, where a major stumbling block is the presence of a mobile disease reservoir, namely patients with Post Kala-azar Dermal Leishmaniasis or PKDL.

To join this lecture, please click on this link: bit.ly/LSID23-Feb.

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