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News & Views

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Interview

Dr A Srividya,
Scientist-E,
ICMR-Vector Control Research Centre,
Puducherry

Upcoming

Lecture Series on Infectious Diseases 2.0:
Lecture 12 by Dr Bontha V Babu,
Director-in-Charge, ICMR-National Institute for Implementation Research on Non-Communicable Diseases, Jodhpur

Editorial

Dear Readers,

The MERA-India team brings you the thirty-seventh issue of our newsletter, "News & Views".

Anopheles stephensi, a species of mosquito originally from Asia, has invaded urban areas in Africa with a high prevalence of resistance to insecticides. This mosquito can easily adapt to urban environments and is causing rapid increases in infections, especially in the Horn of Africa region. Nonetheless, the fight against malaria continues, with Cameroon becoming the first African country to receive its first shipment of *Mosquirix* malaria vaccine, manufactured by British drug maker GlaxoSmithKline Plc (GSK Plc). This comes after successful pilot programmes in Ghana, Kenya, and Malawi.

In this month's lecture series, Dr S Sriram from the Department of Epidemiology, ICMR-National Institute for Research in Tuberculosis (ICMR-NIRT), Chennai gave a talk on 'Barriers and facilitators towards ending TB in India', with a focus on the estimation of TB prevalence, and increased diagnosis of TB, especially within high-risk groups. The highlights from the informational lecture have been enclosed in this newsletter as a summary.

The "Malaria Scientists to Watch" section encompasses an insightful and enriching interview with a talented biostatistician, Dr A Srividya from ICMR-Vector Control Research Centre (ICMR-VCRC), Puducherry.

The "Research in Spotlight" section summarizes three cutting-edge research articles relevant to malaria. The first article by Ravindar *et al.* focuses on the antimalarial activity of various hybridized triazoles that target multiple stages of the *Plasmodium* life cycle. In the second article, Richie *et al.* review over 30 clinical trials that aim to develop a highly effective vaccine against *Plasmodium* sporozoites. In the third article, Kartal *et al.* suggest using serological surveillance methods for malaria to identify individuals exposed to *Plasmodium vivax*, including asymptomatic carriers.

Further, the "Malaria Through the Lens of Researchers" section showcases an image submitted for the MERA-India Image Competition 2022 by Mr Nirdosh, a PhD scholar affiliated with the Molecular Microbiology and Immunology department at CSIR-Central Drug Research Institute (CSIR-CDRI) in Lucknow.

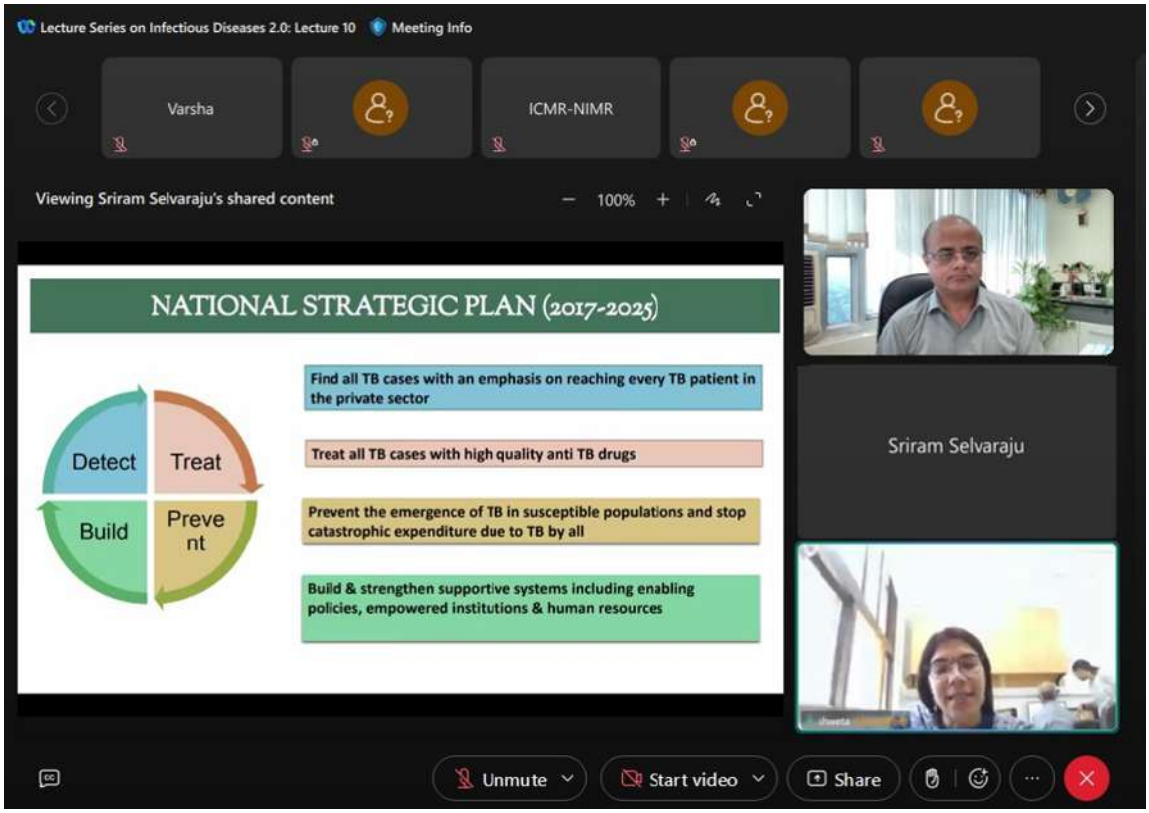
The "Upcoming Events" section covers information on the 12th lecture in the Lecture Series on Infectious Diseases 2.0, to be given by Dr Bontha V Babu, Director-in-charge, ICMR-National Institute for Implementation Research in Non Communicable Diseases (ICMR-NIIRNCD), Jodhpur.

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 Activity

Lecture Series on Infectious Diseases 2.0: Lecture 10 by Dr Sriram Selvaraju



The tenth speaker in the Lecture Series on Infectious Diseases 2.0 was Dr Sriram Selvaraju. Dr Selvaraju currently serves as the head of the Department of Epidemiology at ICMR-NIRT, Chennai. His extensive professional background has been dedicated to studying tuberculosis (TB) prevalence, diagnosis, and control measures. Dr Selvaraju played a crucial role in conducting a national survey on the prevalence of microbiologically confirmed pulmonary tuberculosis in India and actively participated in the national COVID serosurvey during the COVID-19 outbreak. During the lecture, Dr Manju Rahi, Director & Scientist-G, ICMR-VCRC, Puducherry, and Principal Investigator of MERA-India, extended a warm welcome to Dr Selvaraju. Dr Sachin Sharma, Chief Consultant at MERA-India, introduced Dr Selvaraju to the audience, setting the stage for his informative talk.

Dr Selvaraju delivered a presentation on 'Barriers and Facilitators towards Ending TB in India.' He began by providing the audience with fundamental insights into the field, covering topics such as the types of *Mycobacterium tuberculosis*, its evolution, and various Mycobacterial reservoirs. He emphasized the slow division capacity of the pathogen as a reason for the prolonged contagious period before diagnosis. The spectrum of TB, from *M. tuberculosis* infection to active TB diseases, was explained, along with the efficiency of diagnosis methods concerning disease onset. Dr Selvaraju detailed the innate and adaptive

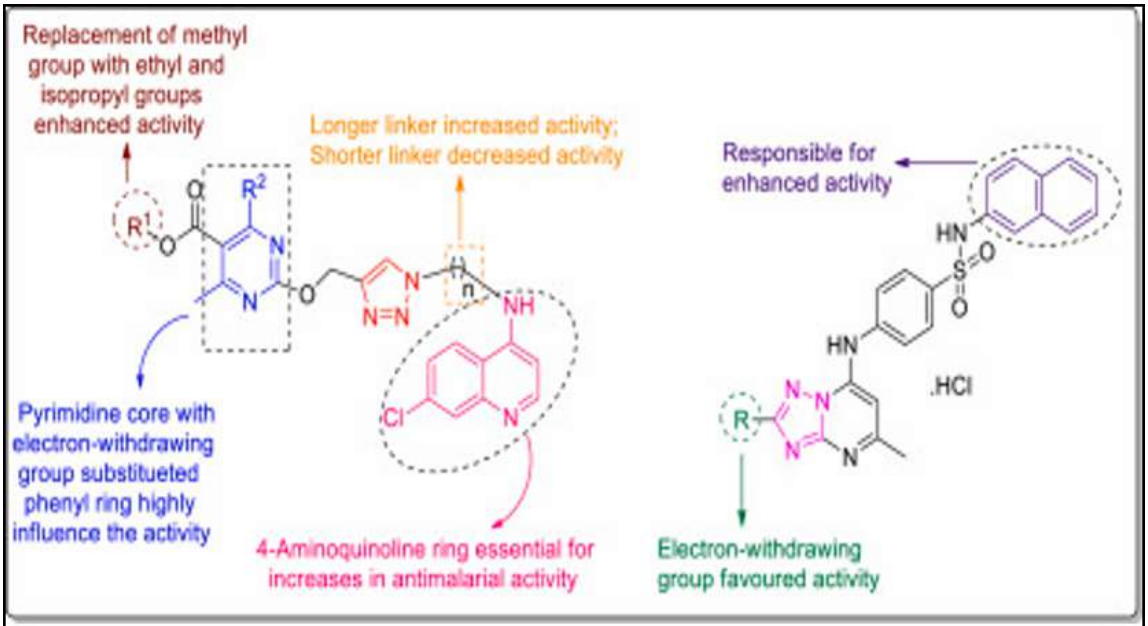
responses of patients against TB and discussed classifications based on diagnosis, anatomical site, and treatment based on drug sensitivity. He pointed out the significant gap between reported and missing TB cases, highlighting the implications for transmission, disease, and mortality. The speaker shared state-wise TB burden data from the National TB prevalence survey in India (2019-2021) and addressed healthcare-seeking behavior. Dr Selvaraju discussed the cascade of care in India's Revised National Tuberculosis Control Programme (RNTCP) and identified contributing factors causing gaps, including patient and health system delays. The lecture covered barriers to ending TB, such as underreporting, uncertain care, drug-resistant and recurrent TB, comorbidities (HIV and diabetes), undernutrition, smoking, elderly alcoholism, and lack of awareness. Dr Selvaraju detailed the efforts of the National Strategic Plan (2017-2025) to end TB, focusing on strategies like Detect, Treat, Prevent, and Build. He highlighted initiatives like Direct Benefit Transfer (DBT) schemes, Nikshay Poshan Yojna, TB Arogya Sathi app, and Nikshay Sampark, along with emphasizing intersectoral engagement.

The lecture concluded with Dr Selvaraju expressing India's commitment and the government's set targets to end TB, highlighting the requirements to achieve this ambitious goal. A question and answer session followed, during which Dr Selvaraju provided insightful responses. Dr Sharma concluded the session with a vote of thanks to the speaker and attendees.

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

Research in Spotlight

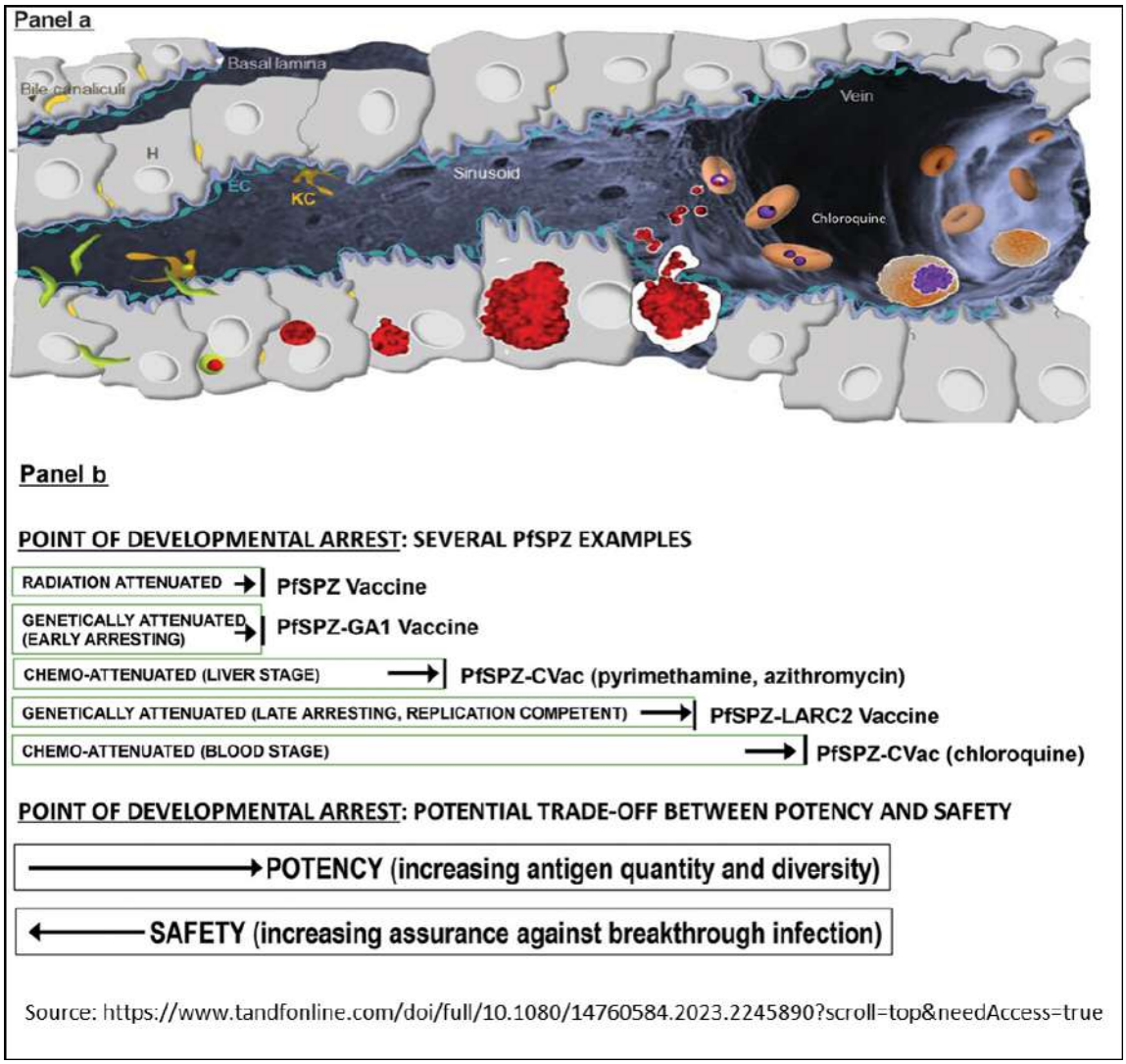
Ravindar, *et al.*, *Eur J Med Chem.* (2023): Triazole hybrid compounds: A new frontier in malaria treatment



Source: https://www.sciencedirect.com/science/article/abs/pii/S022352342300661X

Malaria control faces a serious challenge in the form of drug resistance in malaria parasites, particularly to front-line treatments like artemisinin-based combination therapy. The emergence of resistant clones of *Plasmodium* is worrying since there are no alternative treatment options available for malaria. Therefore, it is urgent to develop novel, cost-effective, and promising antimalarials that can work on dual-stage and multistage parasite life cycles and exhibit excellent activity toward drug-resistant and drug-sensitive *Plasmodium*. Azole-based moieties, especially triazoles, have been extensively studied for their antimalarial efficiency. This study focused on triazoles, which have two isomeric forms, 1,2,3-triazole, and 1,2,4-triazole, with the basic five-membered ring N-heterocyclic scaffolds found in various medicinal drugs. The emergence of triazole hybrid compounds is a breakthrough in malaria treatment, and their potential as effective antimalarial agents has caught the attention of researchers. They are highly effective against both drug-sensitive and drug-resistant strains of *P. falciparum*, making them instrumental tools in resistance-prevalent areas. The combination of the triazole moiety with other pharmacophores has resulted in even greater antimalarial potency. This approach has the potential to overcome existing resistance mechanisms and provide a more sustainable solution to malaria treatment. This review provides a comprehensive study of various hybridized triazole derivatives as promising antimalarial and antiplasmodial agents.

Richie *et al.*, *Expert Rev Vaccines.* (2023): Sporozoite immunization: innovative translational science to support the fight against malaria

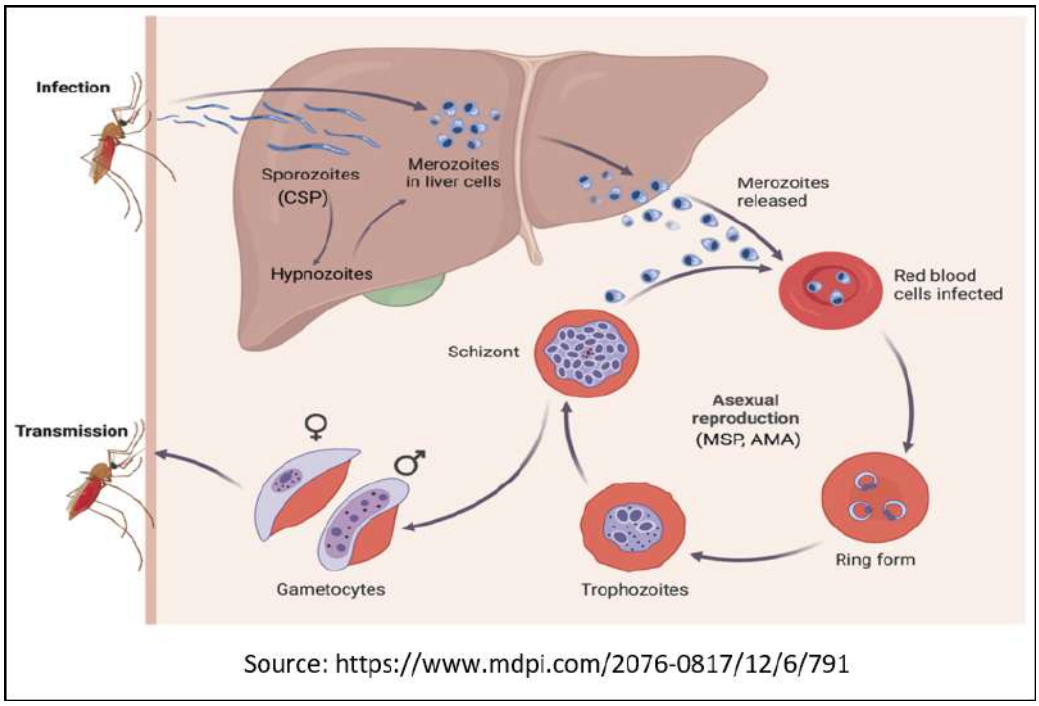


Progress against malaria has stalled in the countries most burdened by this disease, particularly in sub-Saharan Africa. This suggests that current control measures are insufficient. Therefore, there is a need for a new tool in the fight against the malaria parasite, such as a vaccine with high-level efficacy against infection. To achieve regional malaria elimination, mass vaccination programs are required that reach enough of the population to achieve herd immunity. Sporozoites (SPZ) are the parasite stage transmitted by *Anopheles* mosquitoes to humans. They are the only vaccine immunogen achieving >90% efficacy against *Plasmodium falciparum* (Pf) infection. This review describes over 30 clinical trials of PfSPZ vaccines. The primary objective since the inception of development efforts has been to create PfSPZ vaccines that are well-tolerated, safe, and prevent Pf infection in over 90% of recipients for at least 3 months against heterologous controlled human malaria infection (CHMI) and over 90% for at least 2 years without boosting against genetically and antigenically diverse naturally transmitted malaria parasites in Africa. PfSPZ vaccines are aimed at preventing both infection and transmission, not just the disease.

Therefore, they are designed to be deployed in mass vaccination programs to block transmission and eliminate malaria from defined geographic areas. Progress alongside this improvement pathway has required innovation in PfSPZ manufacturing, stabilization, course of administration, medical trial assessment, and genetic manipulation of Pf parasites.

According to the reviewers, the first-generation, radiation-attenuated PfSPZ vaccine was well-tolerated, safe, and provided protection for at least two transmission seasons, with a vaccine efficacy of 50-60% in the field in Africa. The second-generation, chemo-attenuated PfSPZ vaccine induced 100% vaccine efficacy against heterologous CHMI at three months after the last dose. However, it has not yet been adequately assessed for durable vaccine efficacy in the field. Additionally, the second-generation PfSPZ vaccine can cause significant adverse events on days 7 and 8 after the administration of the first dose, unless an anti-inflammatory drug such as ibuprofen is taken. It could also cause severe malaria if chloroquine is not absorbed or taken properly, making it less than ideal from a tolerability and safety perspective. To achieve the tolerability and safety of PfSPZ Vaccine, a third-generation, late liver stage-arresting, replication-competent (LARC), genetically-attenuated PfSPZ will undergo clinical trials to eliminate the potential risks and side effects of the second-generation PfSPZ in 2023-2024. The reviewers envision that the third-generation PfSPZ-LARC2 Vaccine will be licensed for use in travelers and women of childbearing potential.

Kartal, *et al., Pathogens.* (2023): Using Serological Markers for the Surveillance of *Plasmodium vivax* Malaria: A Scoping Review



P. vivax is a type of malaria that is difficult to diagnose using the current microscopy method due to its low parasitemia. Identifying and treating asymptomatic cases is crucial for malaria elimination, but this is not possible with the current diagnostic tools. *P. vivax* also has hypnozoites, which are dormant liver-stage parasites that can cause recurring malaria infections. Since hypnozoites do not cause any clinical symptoms and cannot be detected using current diagnostic tools, they can remain in the liver for extended periods and contribute to up to 80% of *P. vivax* blood-stage infections. This review suggests that serology is a possible solution to overcome the limitations of blood-stage antigen detection-based diagnostics. This method involves screening individuals for antibodies to specific *P. vivax* protein antigens rather than screening for the presence of the parasite itself. Seropositivity can be used as an indirect marker of exposure to *P. vivax*, which can help identify asymptomatic individuals and supplement the standard surveillance methods.

To make serosurveillance an effective tool, various combinations of serological exposure markers should be explored and validated for different transmission contexts. Standardization of serological methods, including the identification of antibody cut-off thresholds, is also necessary. The cross-reactivity of markers and antibodies between species should be further explored and characterized. Implementing serosurveillance in the context of malaria can be challenging since health policies vary across regions. However, studies have identified bottlenecks and made recommendations for improving *P. vivax* health policies. It is also essential to maintain surveillance systems to prevent the resurgence or reintroduction of malaria, particularly in pre-elimination regions. As areas move closer to elimination, serological testing can be a helpful tool as it requires fewer resources to maintain the surveillance system while providing useful results.

Malaria Scientist to Watch:
An interview with Dr A Srividya

Dr A Srividya
Scientist-E,
ICMR-Vector Control Research Centre,
Puducherry

1. Can you elaborate on the specific statistical methods you have employed in your research to analyze epidemiological data related to vector-borne diseases?

Apart from applying the basic statistical methods to the vector-borne diseases (VBD) data, I fitted the zero-truncated negative binomial distribution to the microfilaria counts in humans to understand the over-dispersion in its distribution. As for understanding the factors associated with the occurrence of a disease or intensity of infection, I have applied multivariate logistic regression for binary data and Poisson and Negative binomial regression models to model the count data. Generalized additive models (GAM) with spatial components were applied to model the spatial distribution of filarial disease prevalence to assess the burden of lymphatic filariasis. As for meta-analysis, I have used random effects and mixed effects models to account for the study level covariates and to describe the sources of heterogeneity. Spatio-temporal modelling was currently applied to predict visceral leishmaniasis outbreaks based on the disease cases and environmental factors as predictors. Multilevel models accounting for the contextual factors were applied for disease mapping and longitudinal data analysis of data related to filariasis. Now I am looking forward to learning and applying more advanced modelling techniques that would help in understanding and modelling the transmission dynamics of VBDs better.

2. In your work on the development of sampling strategies, particularly for human and vector sampling, what factors do you consider crucial for ensuring the reliability and representativeness of the samples?

The most crucial factors that will ensure the reliability and representativeness of the samples are (i) the strict adherence to the sampling protocol and the steps described to select the samples from the study area and (ii) using trained personnel (be it for testing samples or interviewing people) and the appropriate tool to collect the data/information.

3. What challenges have you encountered in conducting assessments at the district level, and how have you addressed these challenges in your research?

Only in very few of the districts where I worked, I had a couple of challenges, one of them being the lack of knowledge to understand/speak the local language which led us to depend on the local health staff while conducting the assessments. We realized that the presence of

the local health worker assisting the team (with little knowledge of the local language) did have a bearing on the responses we collected from the participants. However, we could not avoid utilizing their services as we needed their assistance as they were the community's contact person and their help was needed for identifying households/individuals for blood/coverage surveys.
In such situations, I made sure that one of the team members (in all the teams) lured out the local health worker from the household/individual from whom we were gathering information so that we get the correct unbiased information from the participant.

4. How do you envision the role of statistical analysis in improving the overall effectiveness of public health programs targeting vector-borne diseases?

The advanced statistical models that are built to predict or forecast the trend and the outbreaks of VBDs with appropriate easy to use of visualization tools could be a game changer as they could be used by the program authorities to visualize the impending outbreaks of VBDs and take appropriate action at the right time

5. In your opinion, how substantial is MERA-India's contribution in aligning with India's objective of eliminating malaria?

MERA-India has been on the right track as it has provided the opportunity to work on the research needs that will help accelerate malaria elimination, which is currently in its last lap in our country. Starting from funding for most needed operational research studies to conducting online lecture series by eminent global malariologists, it has helped us to understand our current status in achieving malaria elimination and the challenges that we may face while achieving the same. I think MERA-India has contributed substantially in imbibing knowledge on Malaria to the young researchers and medical fraternity, and also has shown the way to move forward by identifying the gaps that need to be addressed, so as to expedite malaria elimination in our country.

Malaria Through the Lens of Researchers

In this current edition, we are featuring another selected entry from the MERA-India Image Competition 2022. This submission comes from Mr Nirdosh, a PhD scholar of Dr Satish Mishra's laboratory, affiliated with the Molecular Microbiology and Immunology department at CSIR-CDRI, Lucknow

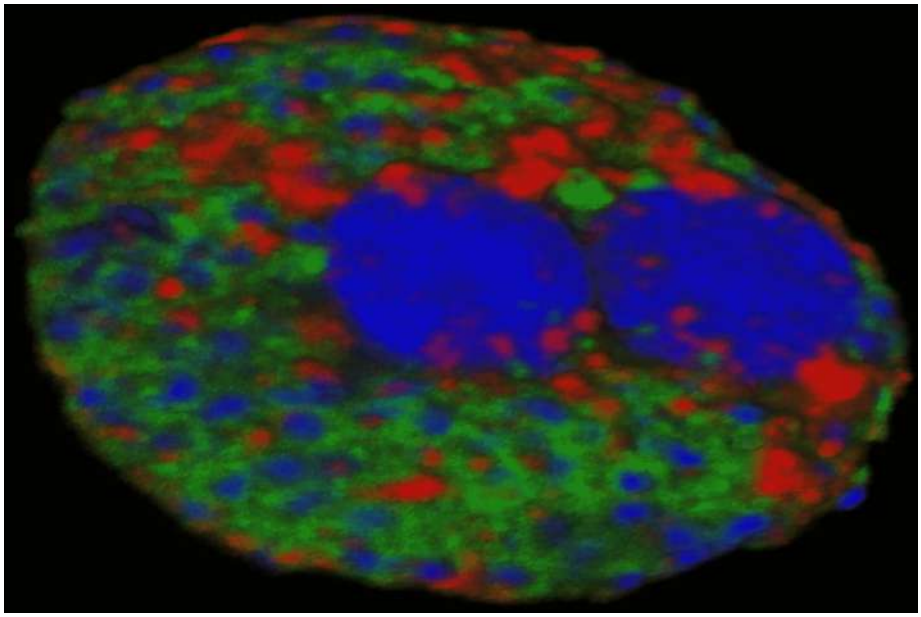


Image title: "Merosome at 65h post-infection stained with Alexa 488, 594, and Hoescht"

A brief description of the image is as follows:
This is an image of a merosome at 65h post-infection stained with Alexa 488, 594, and Hoescht. The image was captured at 100X in an Olympus confocal microscope (CDRI-intravital facility). This is a 3D composite of a Z-stack with an optical slicing gap of 1 micron. The two large blue blobs are the remains of the degraded host cell nucleus and the small blue spots are parasite nuclei. Green is MSP1 representing individual merozoite membranes and red is the remaining UIS4 after successful and complete PVM rupture which occurs just before merosome formation.

Upcoming Event

Lecture Series on Infectious Diseases 2.0: Lecture 12 by Dr Bontha V Babu

The 12th and concluding lecture in the ICMR-NIMR and MERA-India "Lecture Series on Infectious Diseases 2.0," will be delivered by Dr Bontha V Babu, Director-in-charge, (ICMR-NIIRNCD), Jodhpur. In addition, Dr Babu is the Head of the Socio-Behavioral, Health Systems & Implementation Research Division at the headquarters of the Indian Council of Medical Research in New Delhi. He is an implementation research scientist with PhD in anthropology and a post-graduate diploma in applied statistics, received from Andhra University, Visakhapatnam, India. He has expertise in community-based interventions for health promotion and disease prevention with extensive knowledge in disease control program development and evaluation, cultural epidemiology and ethnography, research and program management, training, health education, and communication strategies. He has published approximately 180 papers in national and international journals and is affiliated with several professional organizations and journals.

More information on the lecture will be made available through the ICMR-NIMR and MERA-India's official website (https://meraindia.org.in/) and social media accounts. Be sure to keep an eye out on these platforms to stay informed about this event. We look forward to your participation in this upcoming session.

To receive regular updates about the events being organized by MERA-India, please subscribe at https://www.meraindia.org.in/event_sub.

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