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MERA-India Newsletter 'News & Views'

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University of California, USA

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Editorial

Dear readers,

MERA-India team presents to you the eleventh issue of our newsletter.

To mark the World Mosquito Day on 20th August, MERA-India organized a Basic Entomology Training at NIMR, Delhi for all the NIMR PhD students. The entomology experts at NIMR taught the students about the various aspects of mosquito biology, and vector control. The students were also given live demonstrations about the identification of various mosquito species and the different life cycle stages.

NIMR and MERA-India launched a “Distinguished Lecture Series” last month. The first speaker of the series was world-renowned structural biologist, Professor Sir David Stuart from the University of Oxford who delivered a lecture entitled “The changing antigenic anatomy of SARS-CoV-2 spike”.

The third lecture of the “Lecture Series on Infectious Diseases” was delivered on 24th August 2021, by Dr Manu Prakash from Stanford University on the topic “Frugal Science: Reimagining the role of technology in global health, science education and disease monitoring”.

In the ‘Guest Commentary’ segment, Prof Pankaja Raghav and Dr Harimadhav Viswanathan have written about the community engagement in India for malaria elimination by 2030. For the ‘Malaria Scientists to Watch’ section, we interviewed Dr M Anitha Rani (Professor, Community Medicine, Sri Ramachandra Institute of Higher Education and Research, Chennai) and Dr Nafis Faizi (Scientist-E, ICMR-NIMR, Delhi).

In the ‘Research in Spotlight’ section, we have highlighted four recent publications in malaria research. In the study by Summers R. *et al.,* published in Cell Chem Biol., the authors have identified the target of two antiplasmodial compounds using genomics and biochemical approaches. In the study by Abdrabou W. *et al.,* published in Nat Metab., host metabolome changes have been analyzed to provide mechanistic insights into the pathways and processes altered after the malaria infection. In the study by Neves B J. *et al.*, published in PLoS Comput Biol., the authors have used modelling and deep-learning approaches to identify novel anti-malarial compounds. In the study published in Lancet Microbe by Whittaker C. *et al.,* the authors conducted a systematic review and meta-analysis using the global malaria prevalence data to identify the determinants of submicroscopic infection prevalence. We compliment the authors of these studies on their novel findings and hope that our readers will find these articles informative to read.

In the ‘Upcoming Event’ section, we have provided the details about the lecture in the “Distinguished Lecture” series by Professor Elizabeth Ann Winzeler, the current Director of Malaria Drug Accelerator (MalDA), on 24th September 2021, on the topic “The Malaria

Drug Accelerator- collaborative approaches to new medicines”

We hope you will enjoy reading this issue.

For any feedback or suggestions towards the content of the newsletter, please write to us at meranewsletter@gmail.com.

With best wishes
MERA-India team

NIMR Activities:
Basic Entomology Training for NIMR PhD students

To commemorate the World Mosquito Day on 20th August, MERA-India organized a one-day training in basic entomology at NIMR Delhi, for all the NIMR PhD students.

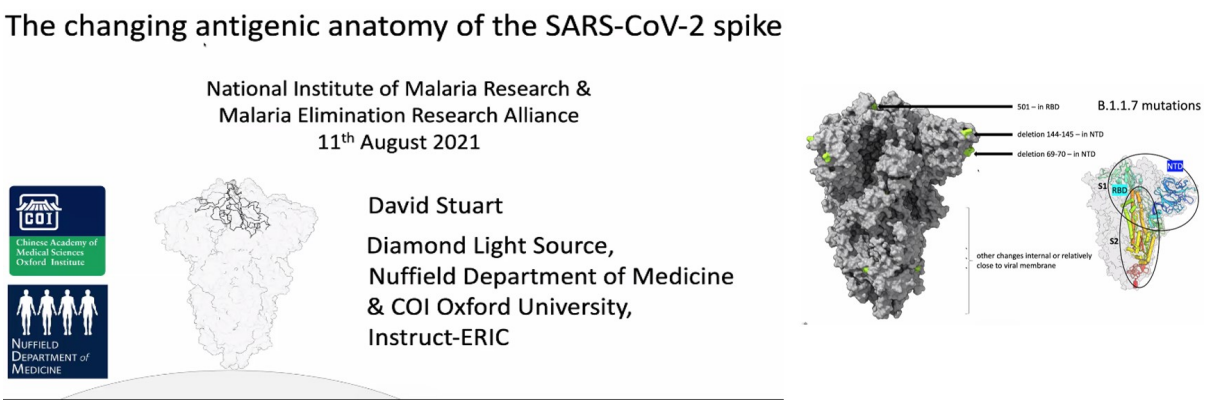
In this highly interactive training, the entomology experts at NIMR taught the students about the various aspects of mosquito biology, the prevalent malaria vectors in India, identification of different mosquito species and the different approaches for vector control & malaria surveillance.

The presentations were followed by live demonstrations of various life stages of the different mosquito species and a visit to the NIMR insectary to learn about the mosquito breeding for research purposes.

A quiz was organized at the end of the training session, in which the students participated enthusiastically.

The Director NIMR encouraged the students to actively participate in such training events. The event concluded with the distribution of participation/ appreciation certificates by Director NIMR to all the students and the training staff.

Distinguished Lecture by Professor Sir David Stuart



NIMR and MERA-India started a virtual “Distinguished Lecture” Series, in which renowned scientists from across the world would be invited to deliver a lecture and share their research.

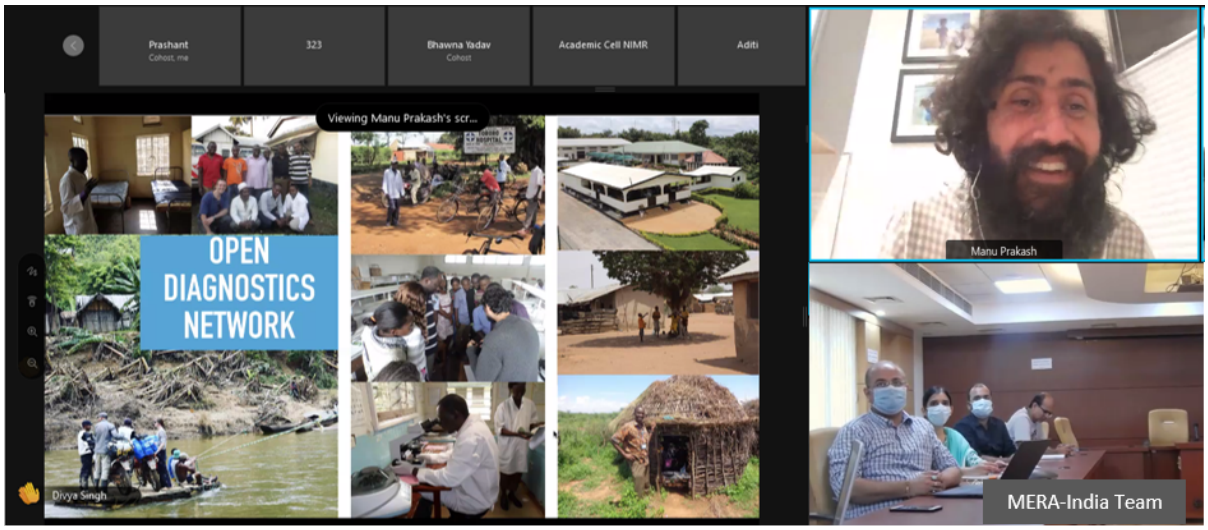
The first lecture of the series was delivered on 11th August 2021 by a world-renowned structural biologist, Professor Sir David Stuart from the University of Oxford, who has made seminal contributions in the field of viral crystallography. A large number of researchers from all over the world attended the lecture. The Director NIMR, Dr Amit Sharma introduced the speaker and thanked him for accepting the invitation to speak in the series.

Professor Sir David Stuart started the lecture by highlighting the role and impact of structural biology in different stages of COVID-19 pandemic response right from pathogen characterization to development of diagnostics & vaccines and understanding the emergence of variants. He then explained the structure and different conformations of the spike protein, and the interaction of spike protein receptor binding domain (RBD) with human ACE2 receptor. He next showed the data where anti-spike proteins from different patients were isolated and expressed from single B-cells. An analysis of these ant-spike proteins showed that the response was polyclonal, however, anti-RBD antibodies were found to be more potent in neutralizing the virus. He further explained how structural biology has led to deciphering the effects of the spike protein mutations in different SARS-CoV-2 variants, in terms of the virus binding to the host ACE2 receptor as well as the virus neutralization by the host antibodies.

The lecture was followed by answers from the speaker to the questions from the audience. The lecture concluded with a note of thanks from Dr Amit Sharma to the speaker and the attendees.

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

Lecture 03 of Lecture Series on Infectious Diseases



The third lecture of the NIMR & MERA-India virtual “Lecture Series on Infectious Diseases” (June 2021-May, 2022), was delivered by Dr Manu Prakash, Associate Professor, Stanford University on the topic “Frugal Science: Reimagining the role of technology in global health, science education and disease monitoring”.

Dr Sachin Sharma, Chief Consultant, MERA-India welcomed everyone and introduced the speaker. In his lecture, Dr Prakash talked about the philosophy of frugal science, to build thoughtful, simple and creative solutions, which are affordable and can be used in resource-limited settings, even under a tree.

He talked about the working and applications of several such powerful and cost-effective tools, built by his group on the principles of fundamental science for use in infectious disease research, diagnostics and surveillance. He described a human-powered low-cost centrifuge built upon the science behind the oldest toy in the history of mankind; Abuzz-a cell-phone based acoustic detection system for mosquito species identification; Vector Chip- to track the pathogen dynamics in the mosquitoes; BiteOscope: an AI-driven tool to study mosquito biology in a quantitative manner; Octopi: automated field-diagnostic for malaria built on the principles of flow cytometer and microscopy; SnapDx: a LAMP-based COVID-19 molecular diagnostic tool for home testing; and, foldscope: a low cost microscope.

He also urged the scientific community to create an inclusive environment by sharing the fruits of their research and science with communities around the world to build a future driven by scientific insights.

The lecture was followed by an interactive session with the audience and answers to the questions. The session ended with a note of thanks from Dr Sachin Sharma to the speaker and the attendees.

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

Guest Commentary

Community Engagement in India for achieving the Zero malaria target by 2030

Prof Pankaja Raghav[1] and Dr Harimadhav Viswanathan[2]

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The history of malaria is as old as the history of mankind. The first description of the disease has been in Chinese medical records dating back to 2700 BC. Being one of the most widespread diseases, it has taken away the life of many and even played a role in the disappearance of some nations and major military defeats. In the year 2019, 409,000 malarial deaths were reported in around 87 malarial endemic countries with an estimated 229 million cases. India, with a population of 1.3 billion accounts for 2% of the global malarial case burden and 2% of the global malarial death burden, with 52% of all malarial deaths outside Sub-Saharan Africa. (1)

Community engagement in India for malaria dates back to the 1980s when DDT and malathion resistance came up and the Malaria Research Centre ensured community participation for biological and environmental methods to control the disease through health education in rural areas in India. The idea turned out to be a huge success in controlling the disease, but there were no efforts to sustain the initiative. The main focus currently, for reaching the goal of Zero malaria target-2030 should be sustaining the community participation. Thus for successful implementation of malaria elimination, community engagement becomes an integral part. The prevention strategies for any disease can be successful only when a community understands the merits of prevention and for that understanding people's beliefs and behaviour is foremost. Even though the significance of community engagement in the successful control and elimination of many infectious diseases has been well established, its role in malaria control and elimination programmes has only been marginal. Apart from traditional practices e.g. theatre, print & electronic media, focus group discussion, in-person communication like doctor-to-patient communication, etc., in this era of technology, the use of social media for sharing IEC materials and telecast of such activities in local television channels and newspapers also play a pivotal role. (2)

Depending on the issue to be addressed and the methods available, the strategy for community participation can be selected. Social and behaviour change communication (SBCC) is a common strategy for community involvement, it aims to share the knowledge and assist communities in changing specific behaviours to obtain better health outcomes. These tactics can reach the target population through a number of communication

channels, ranging from interpersonal to mass media. And this can help in raising malaria awareness and boosting the engagement of community. Many countries have found it beneficial to teach community members in remote areas where access is limited, to do the fundamental health duties. Community surveillance and information-sharing are frequently found to be beneficial because the people who know the most about community health issues are often the people who live in the communities themselves.

Volunteer groups from the community are formed at block levels to run a vector control programme at ground levels with the goal of identifying mosquito breeding sites and to ensure that local people have access to preventive measures like bed nets. Similarly, higher authorities can't always be sure that their investments are meeting the needs of the target population. A strong community engagement can ensure long-term reductions in transmission of the disease, by eliminating health disparities, and improving the effectiveness of various interventions. These interventions can have benefits that go beyond health, depending on the strategy that is chosen. Participants usually gain skills and information; grassroots advocacy can help local governments respond more quickly to community needs; and collaborations between community-based organisations, corporations, and government institutions can improve intersectoral collaboration.

Even individual interventions need community participation; while indoor residual spraying requires residents to accept that their home will be sprayed as per the guidelines, requiring a community to sleep under bed nets necessitates a change in daily habits and sleeping habits. When the community is involved, some treatments simply work better. Environmental management, such as the eradication of mosquito breeding areas, is frequently done from the top down. Experts enter in an unfamiliar region, locate and treat any breeding places they can find, and then leave. When the community gets involved, they'll be better able to figure out where the mosquitos that bite them on a regular basis originate from and ensure that the site is properly managed so that the problem doesn't resurface the next time water collects. (3)

Malaria elimination programmes are heavily influenced by social and behavioural factors based on traditional beliefs and social conventions, which may limit access to preventive and treatment services for specific community groups. To achieve long-term effects, many of the strategies used to combat malaria today rely on community acceptance, active engagement, and ownership of programmes. Communities that are aware of and worried about malaria can participate actively in making more equitable decisions and gaining visibility of local concerns affecting the illness, in addition to making programmes more effective. The key success of any disease elimination depends on the support and participation of the people most affected by it. These communities have the most to gain in terms of reduced expenses on health conditions, improved general health, better performing schools and less burden on health care systems. To conclude, there is no “one size fits all” solution to address the issue of malaria. Multipronged strategies involving health-care related sectors need to be employed for malaria control as it cannot be controlled by the health sector alone. An integrated vector control approach will only be useful, if they are effectively used by communities.

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2. Ghosh S, Rahi M. Malaria elimination in India —The way forward. Journal of Vector Borne Diseases. 2019;56(1):32

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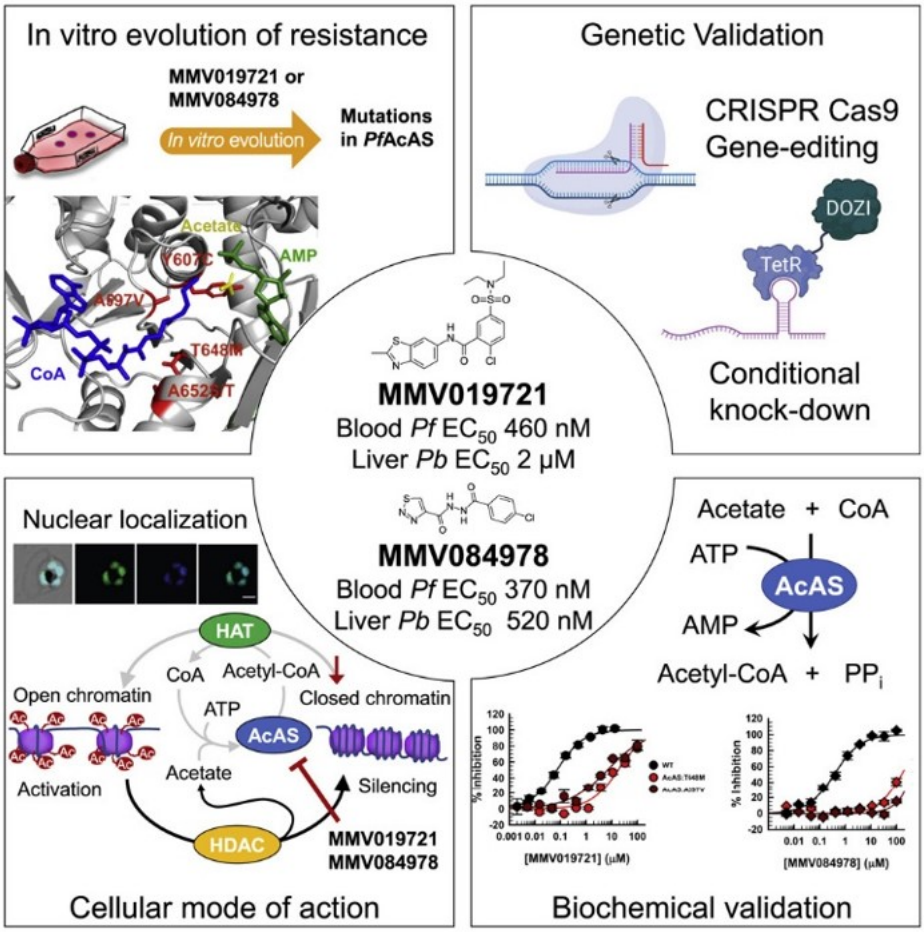
Research in Spotlight

Summers R L. *et al.*, *Cell Chem Biol.*, 2021: Chemogenomics identifies acetyl-coenzyme A synthetase as a target for malaria treatment and prevention

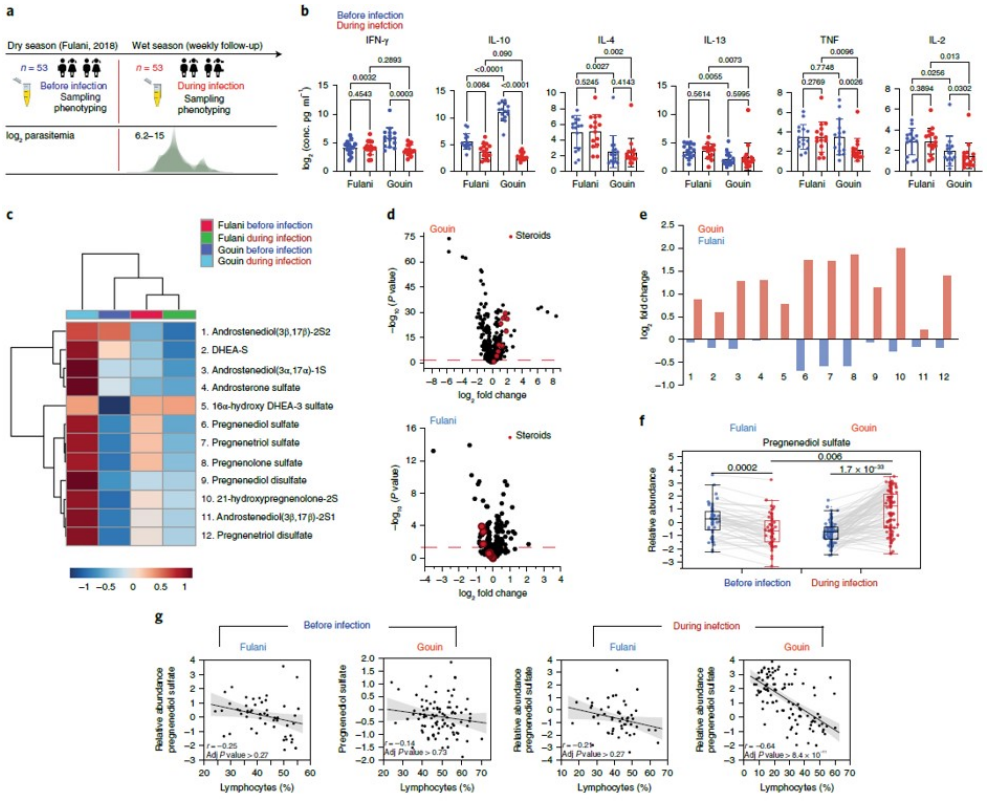


Source: https://pubmed.ncbi.nlm.nih.gov/34348113/

In this study, the authors have used a combination of genetic, and biochemical approaches to identify the target of two antiplasmodial compounds, MMV019721 and MMV084978, effective against both the liver and blood-stages of the plasmodium parasite. The authors conducted an *in-vitro* evolution experiment to isolate the resistant clones upon exposure to these two drugs. Whole-genome sequencing of the resistant clones led to the identification

of mutations in putative acetyl-CoA-synthetase (PfAcAS). The findings were validated by generating and analyzing the conditional PfAcAS mutants, which demonstrated the essential role of PfAcAS in the asexual growth of the parasite. Metabolic profiling and various biochemical assays showed that these two antiplasmodial compounds selectively inhibited PfAcAS by preventing CoA and acetate binding.

Abdrabou W. *et al.*, *Nat Metab.*, 2021: Metabolome modulation of the host adaptive immunity in human malaria

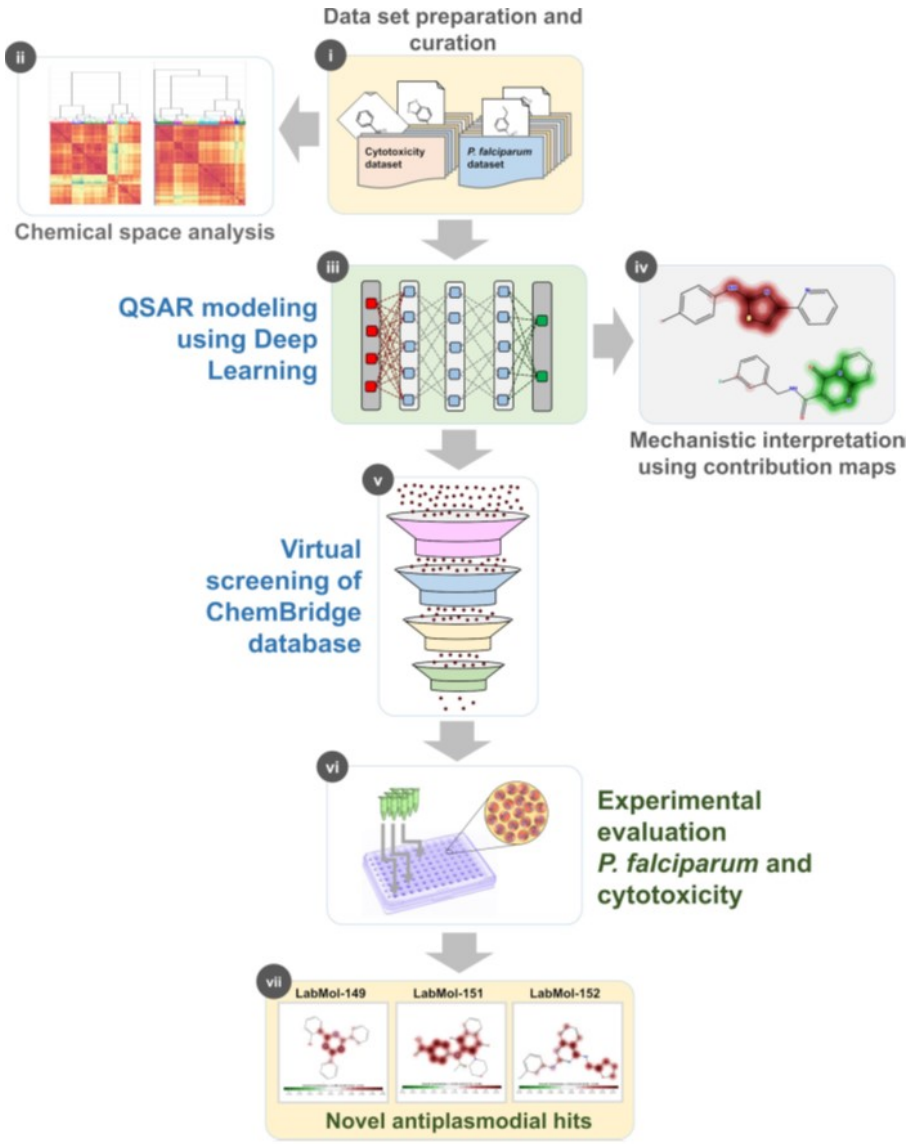


Source: https://pubmed.ncbi.nlm.nih.gov/34113019/

Blood stage *Plasmodium falciparum* hijacks the host's metabolism for its own survival, growth and proliferation. Authors of this article studied the longitudinal *in vivo* metabolic profiling to understand the changes in metabolome in inter-ethnic groups and to provide mechanistic insight into the pathways and processes altered after the infection. They analyzed high-resolution serum metabolomic profiles from Gouin (high malaria-susceptible) and Fulani (low malaria-susceptible) children and identified 92 parasitaemia-associated metabolites that affect host adaptive immune responses. Further analysis revealed a major perturbation in endogenous steroid levels, in particular the pregnenolone steroids. Elevated levels of these steroids were associated with an immunosuppressive effect on T cells in response to *P. falciparum* malaria antigen stimulation. Interestingly, the steroid levels dropped during the infection in less clinically susceptible and more

immunologically responsive Fulani group children. It is yet to be identified as to which factors trigger or alter steroidogenesis in these two groups.

Neves B J. *et al.*, *PLoS Comput Biol.*, 2020: Deep Learning-driven research for drug discovery: Tackling Malaria

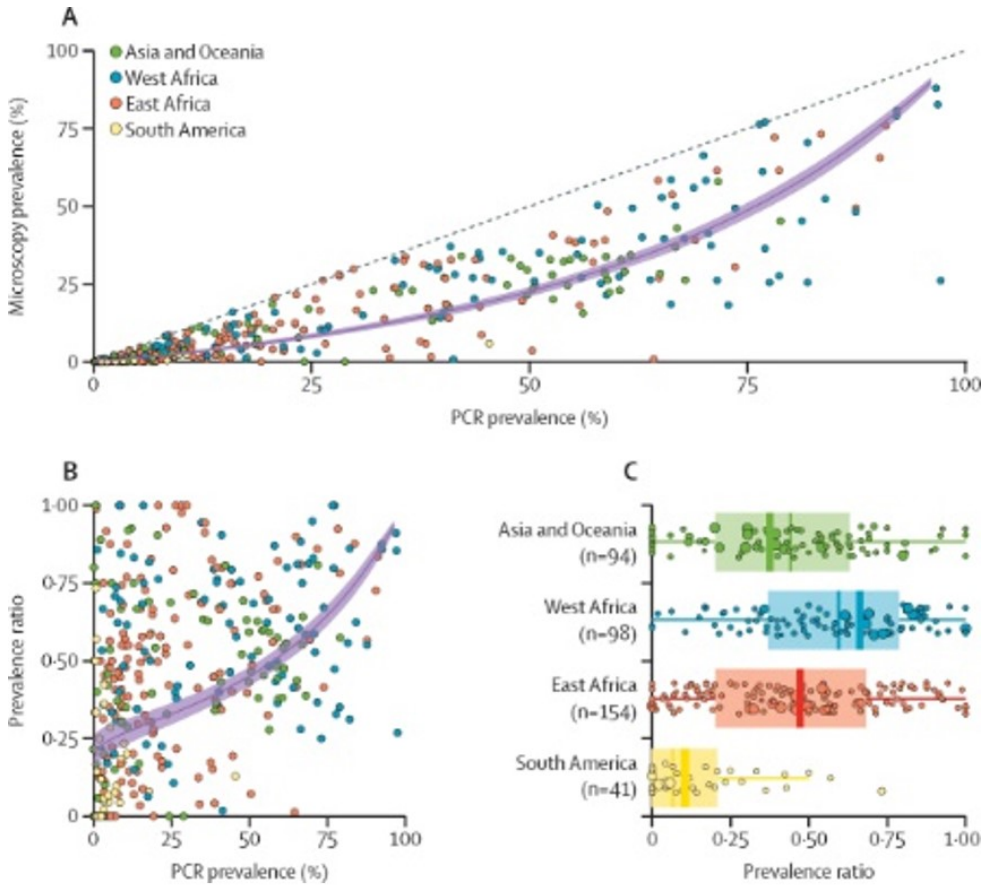


Source: https://pubmed.ncbi.nlm.nih.gov/32069285/

The emergence of parasite resistance to antimalarial drugs is a daunting challenge in malaria treatment. The authors of this study discovered two new compounds, i.e., LabMol-149 and LabMol-152, which might be potential next-generation antimalarial agents. They developed binary and continuous Quantitative Structure-Activity Relationship (QSAR) models implementing Keras and Tensorflow to predict the antiplasmodial activity and cytotoxicity of compounds from the ChEMBL database (CHEMBL2366922 and CHEMBL614822). Applying these models for virtual screening of a large set of compounds

from ChemBridge and certain filtering criteria led them to select five candidate compounds. In vitro evaluation of these compounds against asexual blood stages of *P. falciparum* and multi-drug resistance (W2) strains indicated only two compounds (LabMol-149 and LabMol-152) were potent in inhibition of parasite growth and low cytotoxicity in mammalian cells. Future directions of this study include optimization of compound's structure for higher potency and selectivity, determination of compounds' action stage in the asexual life cycle of *P. falciparum*, and in vivo assays.

Whittaker C*et al.*, *Lancet Microbe*, 2021: Global patterns of submicroscopic *Plasmodium falciparum* malaria infection: insights from a systematic review and meta-analysis of population surveys



Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8332195/

In this study the authors conducted a systematic review and meta-analysis using the global malaria prevalence data from 2010-2020, (cases reported using both microscopy and PCR), to identify the determinants of submicroscopic infection prevalence. The study aimed to explore undetected yet low-density infections, for which the drivers are still unclear. The authors first compared the prevalence of infection by PCR vs microscopy in 267 prevalence survey pairs of 551 cross-sectional global surveys. Using Bayesian Markov

chain Monte Carlo based framework model fitting, it was found that the low transmission areas of South America have the highest prevalence rate of submicroscopic infection, whereas it is less in West African surveys where transmission of *P. falciparum* is high. The study also examined the historical transmission intensity for determining the size of the submicroscopic reservoir majorly in four regions: Asia and Oceania, West Africa, East Africa and South America. It observed a small yet significant influence of seasonality, with fewer submicroscopic infections observed in the wet season than the dry season.

Malaria Scientists to Watch

An interview with Dr M Anitha Rani

Dr M Anitha Rani

Professor

Department of Community Medicine
Sri Ramachandra Institute of Higher Education and Research, Chennai

1. *Please share with our readers your journey from being a young science student to your current position in the Department of Community Medicine at Sri Ramachandra Medical College & Research Institute.*

I started my career as an Assistant Professor in the Department of Community Medicine at Sri Ramachandra Institute of Higher Education and Research. In addition to teaching community medicine to medical and paramedical students, I had the privilege of working on research projects under the guidance of Professor B.W.C. Sathiyasekaran, an eminent epidemiologist in India. Inspired by his teachings on research methodology, I slowly developed a passion towards research. I got trained in sample size calculation, epidemiological study designs and qualitative research from the Department of Biostatistics, Vellore CMC. I started taking up individual research projects and received GATE (Growth advancement towards excellence) funding from SRIHER and funding from THE UNION, Paris for an operational research project on nutritional interventions in schools. I started providing guidance to research scholars, students and faculty members of our university and outside institutions, slowly mastering the intricacies in research. Next, I started my own research guidance centre to guide the medical fraternity in their research process. I have been appointed as a member of research advisory committees in different healthcare institutions and a member in various Institutional Ethics Committees. I have 41

publications to my credit in national and international journals and delivered guest lectures on research methodology topics within and outside the Tamil Nadu state in various academic institutions.

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

Throughout my career, my research focus areas have been mainly lifestyle modifications for the prevention of non-communicable diseases and community based interventions targeting high risk populations. A few years back I started working with a research scholar to evaluate the effectiveness of school-based interventions on the prevention and control of malaria. Being a public health researcher, I clearly understood the importance of community based interventions towards malaria elimination. As part of the national framework of malaria elimination, I am currently involved in a research project on Community behaviour and its determinants in relation to malaria elimination for developing and implementing a scalable community engagement model, with the main objectives of identifying the behavioural barriers of at risk communities regarding acceptance and use of available preventive measures and exploring early and effective health care seeking behaviour towards Malaria.

3. *If you were to pick one scientific discovery that has been crucial to our current understanding of malaria, which one would that be?*

Being a community medicine specialist, developments in malaria vaccine, which is a primary preventive strategy, interests me as a crucial step towards malaria elimination. Malaria is a complex disease that needs multifaceted interventions. A safe, effective and affordable malaria vaccine would help to close the gap left by other interventions such as drug resistance, insufficient IRS spray, ineffective community mobilization strategies etc. Newer malaria vaccine R21 in adjuvant Matrix –M, has shown promising results of up to 77% effectiveness in phase II clinical trial among young children in Burkina Faso, West Africa. R21 is designed to be both more potent and cheaper to produce than the already approved RTS vaccine which has 36% efficacy. R21 vaccine targets the malaria parasite in the sporozoite phase of its life cycle and researchers plan to test R21 in larger trials of 4800 children. As this vaccine shows safety and high levels of efficacy, it’s a promising tool for malaria elimination.

4. *According to you, what is the biggest challenge to malaria elimination in India?*

Most of the challenges in malaria elimination are site specific. A crucial challenge in all high endemic districts is ensuring community participation and community mobilization. Community members’ role in prevention of mosquito breeding in water storage containers, usage of insecticide treated mosquito nets, acceptance of IRS Spray and early health seeking for malaria fever is the vital step towards malaria elimination. Local community leaders and youth volunteers need to be engaged in identifying the challenges for malaria elimination in their area, in planning and execution of malaria intervention strategies. They will be the key change makers to bring in necessary behaviour change in the community. Of course, very strong political commitment is crucial for successful implementation of the

community engagement model.

5. *Apart from science and research, which other activities interest you?*

Early morning meditation and yoga practices keep me fit and healthy and active throughout my day. I like travelling, being with nature, listening to birds chirping and long walks on the beach. Reading books and spending quality time with family members is my all-time favourites. Listening to music during my evening walks is a real stress buster.

An interview with Dr Nafis Faizi

Dr Nafis Faizi

Scientist -E

ICMR-National Institute of Malaria Research, Delhi

1. Please share with our readers your professional journey from being a young science student to your current position as Scientist E in ICMR-NIMR?

As a medical graduate, I was always fascinated with the community and public health and I chose to join the Masters in Community Medicine (MD) programme to pursue a career in academia and research due to my strong interest in public health. Later, I completed a Master in Public Health (MPH) to further strengthen my understanding of core issues in Public Health and Epidemiology. For the last eight years, before joining ICMR-National Institute of Malaria Research (NIMR), I worked as a faculty in Community Medicine at JN Medical College that involved teaching Epidemiology, Health Systems, Health Policy and Demography and other areas of Community Medicine. Being a biostatistics enthusiast, I underwent research trainings from WHO, The Union and Jameel Poverty Action Lab and became the training instructor for the Epidemiological Research Unit in addition to the primary responsibilities.

Over the years, I have researched diverse areas in public health primarily from an epidemiological and health systems lens. I also trained myself as a volunteer teacher for People's Open Access Initiatives for public health postgraduates in LMICs. Apart from my research, I regularly engaged in policy discussions internationally especially on health systems with WHO via Democratizing Global Health Initiative since 2018, intervening in the WHO EB/WHA meetings. I am also a part of the Antibiotic Resistance Coalition through which I engage with WHO and Tripartite agencies (FAO, OIE and WHO) in critical policies around antimicrobial resistance. Given my growing inclination towards joining a full-time

research position, I joined as a Scientist-E at ICMR-NIMR in July 2021.

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

As I often remarked in my classes, if there are two diseases that can teach you public health, they are Tuberculosis and Malaria. Malaria specifically has a long history and mosquito is still the biggest human killer. If we trace the fascinating history of Malaria, as I often did, you find its indomitable position in the past killing the ruthless Genghis Khan at the time. In dire contrast, the same Malaria also inflicted the compassionate Mother Teresa leading to her death later from heart failure. Even if we look at the National Malaria Control Programme launched in 1953, the initial success led to the ambitious National Malaria Eradication Programme in 1958. Eventually, Malaria fought back and had a resurgence in urban areas. Every aspect of Malaria's fight with humans is interesting. Even during Covid-19, the widely used concept of R_0 comes directly from the works of Malaria scientists with Macdonald basing it on Alfred Lotka's work and Ronald Ross's first attempt at Mathematical Epidemiology.

The public health history of Malaria, its programmatic successes and failures, its epidemiological indicators, its ability for resurgence- there is no aspect of Malaria that does not interest a student of Public Health. So, here I am.

3. *If you were to pick one scientific discovery that has been crucial to our current understanding of malaria, which one would that be?*

It is hard to pick one. The most important will always be Ronald Ross's seminal discovery that mosquito causes Malaria. Eventually, public health came to the realization that this is a water related disease rather than air. The other most important discovery was that of artemisinin by Dr Tu Youyou that has saved and continues to save countless lives.

4. *According to you, what is the biggest challenge to malaria elimination in India?*

The biggest challenge in the attempt to eliminate Malaria would be to sustain the gains that have been achieved and progress further in the wake of uneven development at many Malarious areas. Environmental source reduction is critical for many such areas, although chemical and biological source containment have been successful. Eventually, elimination will depend on community based sustainable efforts to reduce larval source reduction apart from other multipronged strategies in place. Fortunately, the challenge of resistance is still not as bad in India as in other parts of the world.

5. *Apart from science and research, which other activities interest you?*

I love reading, cycling and Table Tennis. I treasure the books by Dostoyevsky, Huxley, Bradbury and Tolstoy. I still love debating and quizzing, something that I will tremendously miss, as I no longer work in the university environment.

Upcoming Event

Distinguished Lecture by Professor Elizabeth Ann Winzeler

NIMR and MERA-India are pleased to announce that Professor Elizabeth Ann Winzeler, University of California, and the current Director of Malaria Drug Accelerator (MalDA), would be our next speaker in the "Distinguished Lecture" series. She will be delivering the lecture entitled “The Malaria Drug Accelerator- collaborative approaches to new medicines” on 24th September 2021.

In the lecture, Professor Winzeler will describe the approach to finding high value targets for antimalarial drug discovery and mention some of the highlights of MalDA program, including the collateral characterization of the malaria “resistome,” the set of genes and alleles that are associated with multidrug resistance.

To join this lecture, please click here: https://bit.ly/3Ex5Cdy

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