

Unlocking The Potential Of “Pathogen Box Chemical Library” To Advance Therapeutic Interventions Against Human Malaria



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Zoom

Host: Dr Bi Xuezhi

Seminar Abstract

Over centuries ‘Malaria’ has been a threat to mankind, yet until today it remains a global burden affecting nearly half of the World’s Population. Malaria is caused by Plasmodium parasites and Plasmodium falciparum being the most prevalent malaria parasite. The rapid emergence of drug resistance against frontline antimalarials and lack of vaccines has made it extremely imperative to identify new drugs with novel mechanisms of action. In an attempt to precisely expand this drive, we partnered with Medicines for Malaria Venture (MMV), to reappropriate and repurpose the “Pathogen Box” library (400 compounds) against Plasmodium falciparum infection. Egress or Spread of the malaria parasites from the host cell is a rate-limiting process contributing to parasite proliferation during the infectious cycle. This process is amenable to chemical interferences, thus we developed a systematic, cellular phenotype-based antimalarial screening to facilitate the identification of specific blockers of late-stage intraerythrocytic development of Plasmodium falciparum.

We identified 12 compounds that engaged with the proliferation machinery inhibiting late-stage parasite development and stage transition. Further, we elucidate the mechanism of action (MOA), to identify drug targets for few selected compounds by employing multi-omics approaches involving cell biomechanics, transcriptomics and, proteomics studies. These findings open up the possibility of exploiting and repurposing these compounds for therapeutic development targeting late-stage development and egress against the new variants of malaria that are rapidly spreading across the developing world.

About the Speaker

Dr. Alok Patra has joined the Protein Analytics Team at BTI, A*Star as a Project Scientist. He completed his Doctoral degree from Singapore University of Technology and Design, his PhD project was part of a multi-collaborative initiatives between the infectious disease groups with Singapore universities (SUTD and NTU) and Indian Institute (CSIR- NCL, Pune). For his doctoral thesis, Alok undertook a Omics-based approach to understand mechanisms of action of small molecules belonging to the MMV pathogen box library. Specifically, he conducted transcriptomics and proteomics on human malaria parasites exposed to small molecules selected from a comprehensive phenotype-based screening initiative. Prior to his Ph.D., he worked as Research Associate at NTU working on various Malaria projects involving proteomics and, transcriptomics studies. His expertise is in designing drug discovery pipeline, drug validation methods, mechanism of action (MOA) using multi-omics studies to identify novel drug-targets.