

Bio-data of the Applicant

Dr. V. Arun Nagaraj, Institute of Life Sciences, Bhubaneswar

Investigator Details:

Name: Dr. V. Arun Nagaraj

Designation: Scientist-E

Department: Infectious Disease Biology

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Education Details:

S. No.	Institution	Degree Awarded	Year	Field of Specialization
1	Sri Sankara Arts and Science College, Madras University	B.Sc	1997-2000	Biochemistry
2	JIPMER, Pondicherry University.	M.Sc	2000-2003	Medical Biochemistry
3	Dept. of Biochemistry, Indian Institute of Science, Bangalore	Ph.D	2003-2009	Malaria Parasite Biology

Employment Details:

S. No.	Institution	Position	Year
1	Institute of Life Sciences, Bhubaneswar, India	Scientist-E	Jan 2020 – Till Date
2	Institute of Life Sciences, Bhubaneswar, India	Scientist-D	Nov 2015 - Dec 2019
3	Centre for Infectious Disease Research & Department of	Ramanujan Fellow	Nov 2010 - Oct 2015

	Biochemistry, IISc, Bangalore, India.		
4	School of Biological Sciences, Nanyang Technological University, Singapore.	Postdoctoral Research Fellow	Jan 2010 - Sep 2010

Research Interest:

Malaria causes enormous morbidity and mortality, and poses a serious threat to human health. The emerging parasite resistance against artemisinin and its partner drugs and the mosquito resistance against insecticides together with global warming are of great concern. Despite intense global efforts to roll back malaria, no significant reduction in the global incidence could be achieved since 2015 and in fact, there is a considerable increase in the last four years. Further, India accounts for more than 80% of the malaria cases in the WHO South-East Asia region. My research interest is on developing new therapeutic interventions for malaria by gaining insights into the fascinating biology of *Plasmodium* asexual, sexual and liver stages. The following are the major research initiatives that have been undertaken: 1) Understanding the molecular re-programming events that occur in the asexual, sexual and liver stages of parasite life cycle. 2) Identifying the key parasite factors that are responsible for parasite virulence, disease pathogenesis and host-immune evasion. 3) Understanding the significance of amino acid requirements in the entire life cycle of malaria parasite. 4) Deciphering the molecular mechanisms underlying the development of sexual stages in mosquitoes and exo-erythrocytic stages in liver. 5) Screening phytochemicals for new antimalarials and developing highly-sensitive diagnostic tools for malaria. Delineating the molecular aspects of parasite life cycle and designing strategies to interfere with parasite pathways and homeostasis of host-parasite networks can be explored for new therapeutic approaches to combat malaria and antimalarial drug resistance. The recent work from our laboratory on the role of parasite heme in disease severity and cerebral pathogenesis, and the requirement of a distinctively evolved parasite glutamine synthetase for *P. falciparum* survival, have opened up new avenues of promising targets to prevent malaria mortality and combat artemisinin resistance. Besides publishing the findings in highly reputed journals and filing Indian and International patents, we have taken them forward for clinical trials in humans to prevent mortality due to cerebral and severe malaria.

There is also a parallel attempt to develop new molecules that can be used in the long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) for preventing malaria transmission. This assumes significance in the context of mosquito resistance to major insecticide classes such as pyrethroids, organochlorines, carbamates and organophosphates used for LLINs and IRS. Another interesting aspect that has been pursued is the ability of curcumin to prevent cerebral malaria and parasite recrudescence. A phase II clinical trial funded by DBT to evaluate the safety and efficacy of curcumin with standard therapy in uncomplicated malaria is going to be initiated in collaboration with NIMR. We have also collaborated with start-ups like Jigsaw Biosolutions Pvt Ltd, Bangalore, to develop a highly sensitive PCR diagnosis for malaria detection based on unique Identical Multi Repeat Sequences (IMRS) present in the parasite genome that can detect asymptomatic falciparum infections, crucial in the malaria elimination programs. The entire infrastructure required to perform the cutting-edge research on asexual, sexual and liver stages of malaria parasite have been built over a period of years with indigenous effort. It is worthwhile to mention that only a very few laboratories in the world work on the entire life cycle of malaria parasite. In summary, the research objectives pursued in our laboratory are of societal relevance and they align with the global and national targets set by WHO, PATH, Malaria No More, National Vector Borne Disease Control Programme (NVBDCP), Indian Council of Medical Research (ICMR) etc., in terms of eliminating and eradicating malaria.

Publications

1. Ghosh, S., Kundu, R., Chandana, M., Das, R., Anand, A., Beura, S., Bobde, R.C., Jain, V., Prabhu, S.R., Behera, P.K., Mohanty, A.K., Chakrapani, M., Satyamoorthy, K., Suryawanshi, A.R., Dixit, A., Padmanaban, G. & **Nagaraj, V.A.** (2023). Distinct evolution of type I glutamine synthetase in Plasmodium and its species-specific requirement. *Nature Communications*, 14, 4216. (Corresponding Author)
2. Singh, N., Chatterjee, A., Chanu, W. K., Vaishalli, P. M., Singh C.B. & **Nagaraj, V.A.** (2023). Antimalarial activity of Toona ciliata MJ Roem aqueous methanolic leaf extract and its antioxidant and phytochemical properties. *Journal of Traditional and Complementary Medicine*. <https://doi.org/10.1016/j.jtcme.2023.05.004> (In Press). (Corresponding Author)
3. Anand, A., Chandana, M., Ghosh, S., Das, R., Singh, N., Vaishalli, P. M., Gantasala, N. P., Padmanaban, G. & **Nagaraj, V.A.** (2023). Significance of Plasmodium berghei Amino Acid Transporter 1 in Food Vacuole Functionality and Its Association with

Cerebral Pathogenesis. *Microbiology Spectrum*, 11(2), e04943-22. (Corresponding Author)

4. Chatterjee, A., Singh, N., Chanu, W.K., Singh, C.B. & **Nagaraj, V.A.** (2022). Phytochemical screening, cytotoxicity assessment and evaluation of in vitro antiplasmodial and in vivo antimalarial activities of *Mentha spicata* L. methanolic leaf extract. *Journal of Ethnopharmacology*, 298, 115636. (Corresponding Author)
5. Chandana, M., Anand, A., Ghosh, S., Das, R., Beura, S., Jena, S., Suryawanshi, A.R., Padmanaban, G. & **Nagaraj, V.A.** (2022). Malaria parasite heme biosynthesis promotes and griseofulvin protects against cerebral malaria in mice. *Nature Communications*, 13, 4028. (Corresponding Author)
6. Suravajhala, R., Parashar, A., Choudhir, G., Kumar, A., Malik, B., **Nagaraj, V.A.**, Padmanaban, G., Polavarapu, R., Suravajhala, P. & Kishor, P. K. (2021). Molecular docking and dynamics studies of curcumin with COVID-19 proteins. *Network Modeling Analysis in Health Informatics and Bioinformatics*, 10(1), 44.
7. Padmanaban, G. and **Nagaraj, V.A.** (2020). Hydroxychloroquine - A Relatively Obscure Antimalarial Takes Centre Stage in COVID-19. *Current Science*, 118 (10), 1489-1491.
8. Raju, L.S., Kamath, S., Shetty, M.C., Satpathi, S., Mohanty, A.K., Ghosh, S.K., Kolluri, N., Klapperich, C.M., Cabodi, M., Padmanaban, G. & **Nagaraj, V. A.** (2019). Genome Mining–Based Identification of Identical Multirepeat Sequences in *Plasmodium falciparum* Genome for Highly Sensitive Real-Time Quantitative PCR Assay and Its Application in Malaria Diagnosis. *The Journal of Molecular Diagnostics*, 21(5), 824-838. (Corresponding Author)
9. Dende, C., Meena, J., Nagarajan, P., **Nagaraj, V.A.**, Panda, A.K., & Padmanaban, G. (2017). Nanocurcumin is superior to native curcumin in preventing degenerative changes in Experimental Cerebral Malaria. *Scientific Reports*, 7(1), 10062.
10. **Nagaraj, V.A.**, & Padmanaban, G. (2017). Insights on heme synthesis in the malaria parasite. *Trends in Parasitology*, 33(8), 583-586. (Corresponding Author)
11. Padmanaban, G., & **Nagaraj, V.A.** (2017). Curcumin may defy medicinal chemists. *ACS Medicinal Chemistry Letters*, 8(3), 274-274.
12. **Nagaraj, V.A.**, Mukhi, D., Sathishkumar, V., Subramani, P.A., Ghosh, S.K., Pandey, R. R., Shetty, M.C. & Padmanaban, G. (2015). Asparagine requirement in *Plasmodium berghei* as a target to prevent malaria transmission and liver infections. *Nature Communications*, 6(1), 8775. (First & Corresponding Author)

13. Varadarajan, N.M., Sundaram, B., Subramani, P.A., Kalappa, D.M., Ghosh, S.K., & **Nagaraj, V.A.** (2014). Plasmodium berghei glycine cleavage system T-protein is non-essential for parasite survival in vertebrate and invertebrate hosts. *Molecular and Biochemical Parasitology*, 197(1-2), 50-55. (Corresponding Author)
14. Sundaram, B., Varadarajan, N. M., Subramani, P. A., Ghosh, S. K., & **Nagaraj, V.A.** (2014). Purification of a recombinant histidine-tagged lactate dehydrogenase from the malaria parasite, Plasmodium vivax, and characterization of its properties. *Biotechnology Letters*, 36, 2473-2480. (Corresponding Author)
15. **Nagaraj, V.A.**, Sundaram, B., Varadarajan, N.M., Subramani, P.A., Kalappa, D.M., Ghosh, S.K., & Padmanaban, G. (2013). Malaria parasite-synthesized heme is essential in the mosquito and liver stages and complements host heme in the blood stages of infection. *PLoS Pathogens*, 9(8), e1003522. (First & Corresponding Author)
16. Padmanaban, G., **Nagaraj, V.A.**, & Rangarajan, P.N. (2012). Artemisinin-based combination with curcumin adds a new dimension to malaria therapy. *Current Science*, 704-711.
17. Vathsala, P. G., Dende, C., **Nagaraj, V.A.**, Bhattacharya, D., Das, G., Rangarajan, P. N., & Padmanaban, G. (2012). Curcumin-artether combination therapy of Plasmodium berghei-infected mice prevents recrudescence through immunomodulation. *PloS One*, 7(1), e29442.
18. **Nagaraj, V.A.**, Arumugam, R., Prasad, D., Rangarajan, P.N., & Padmanaban, G. (2010). Protoporphyrinogen IX oxidase from Plasmodium falciparum is anaerobic and is localized to the mitochondrion. *Molecular and Biochemical Parasitology*, 174(1), 44-52.
19. **Nagaraj, V.A.**, Prasad, D., Arumugam, R., Rangarajan, P. N., & Padmanaban, G. (2010). Characterization of coproporphyrinogen III oxidase in Plasmodium falciparum cytosol. *Parasitology International*, 59(2), 121-127.
20. **Nagaraj, V.A.**, Prasad, D., Rangarajan, P. N., & Padmanaban, G. (2009). Mitochondrial localization of functional ferrochelatase from Plasmodium falciparum. *Molecular and Biochemical Parasitology*, 168(1), 109-112.
21. **Nagaraj, V.A.**, Arumugam, R., Chandra, N. R., Prasad, D., Rangarajan, P.N., & Padmanaban, G. (2009). Localisation of Plasmodium falciparum uroporphyrinogen III decarboxylase of the heme-biosynthetic pathway in the apicoplast and characterisation of its catalytic properties. *International Journal for Parasitology*, 39(5), 559-568.

22. **Nagaraj, V.A.**, Arumugam, R., Gopalakrishnan, B., Jyothsna, Y. S., Rangarajan, P. N., & Padmanaban, G. (2008). Unique properties of Plasmodium falciparum porphobilinogen deaminase. *Journal of Biological Chemistry*, 283(1), 437-444.
23. Padmanaban, G., **Nagaraj, V.A.**, & Rangarajan, P. N. (2007). An alternative model for heme biosynthesis in the malarial parasite. *Trends in Biochemical Sciences*, 32(10), 443-449.
24. Padmanaban, G., **Nagaraj, V.A.**, & Rangarajan, P. N. (2007). Drugs and drug targets against malaria. *Current Science*, 1545-1555.
25. Nandakumar, D.N., **Nagaraj, V.A.**, Vathsala, P.G., Rangarajan, P., & Padmanaban, G. (2006). Curcumin-artemisinin combination therapy for malaria. *Antimicrobial Agents and Chemotherapy*, 50(5), 1859-1860. (Equally contributed first author).

Book Chapters

1. Padmanaban, G. and **Nagaraj, V.A.** (2017). Curcumin from turmeric as an adjunct drug? In: Studies in Natural Products Chemistry, Bioactive Natural Products. Edited by Atta-ur-Rahman. Volume 57, 2018, Pages 179-202.
2. **Nagaraj, V.A.**, Rangarajan, P.N. and Padmanaban, G. (2014). Porphyrin Metabolism. Encyclopedia of Malaria. Springer, Edited by Hommel, M. and Kremsner. P.G. 1-11.
3. Padmanaban, G., **Nagaraj, V.A.** and Rangarajan, P.N. (2013). Unique Features of heme biosynthesis in the malaria parasite. Handbook of Porphyrin Science. With Applications to Chemistry, Physics, Materials Science, Engineering, Biology and Medicine. World Scientific Publishers, Edited by Kadish, K.M., Smith, K.M., Guillard, R. and Ferreira, G.C. 27, 168-205.

List of patents granted/filed:

1. A pharmaceutical composition to combat artemisinin resistance in malaria. Indian Patent Application No. 202231018911. (First Inventor)
2. A pharmaceutical composition to combat artemisinin resistance in malaria. PCT Application No. PCT/IN2023/050301. (First Inventor)
3. Griseofulvin as an adjunct drug for the treatment of cerebral and severe malaria. Indian Patent Application No. 202031050934. (First Inventor)
4. Griseofulvin as an adjunct drug for the treatment of cerebral and severe malaria. PCT Application No. PCT/IN2021/051071 (First Inventor)

5. A combination antimalarial drug therapy with curcumin and artemisinin. Indian Patent Application No. 1612/CHE/2005. (One of the inventors)
6. Antimalarial Drug Containing Synergistic Combination of Curcumin and Artemisinin. U.S. Patent No. US 7,776,911 B2. (One of the inventors)
7. Nucleotide sequence, A method and kit thereof. Indian Patent Application no: 893/CHE/2013. (One of the inventors)

Media Coverages:

- 1) Therapeutic interventions to prevent malaria mortality found in Odisha. February 22, 2023. The New Indian Express. <https://www.newindianexpress.com/states/odisha/2023/feb/22/therapeutic-interventions-to-prevent-malaria-mortality-found-in-odisha-2549804.html>
- 2) Indian scientists successfully conduct animal trial of drug for malaria. February 23, 2023. Hindustan Times. <https://www.hindustantimes.com/india-news/indian-scientists-successfully-conduct-animal-trial-of-drug-for-malaria-101677129145983.html>
- 3) “Diagnostics for asymptomatic malaria” published in the Science section of The Hindu BusinessLine and Vigyanprasar dated February 27, 2020. <https://www.thehindubusinessline.com/news/science/diagnostics-for-asymptomatic-malaria/article30933280.ece>
<https://vigyanprasar.gov.in/isw/Diagnostics-for-Asymptomatic-Malaria.html>
- 4) “Indigenous malaria vaccine shows promise in mice studies”, S&T, The Hindu, April 17, 2014. <http://www.thehindu.com/sci-tech/health/medicine-and-research/indigenous-malaria-vaccine-shows-promise-in-mice-studies/article5918997.ece>
- 5) “Knocking down the malaria causing parasite”, S&T, The Hindu, August 22, 2013. <http://www.thehindu.com/sci-tech/health/knocking-down-the-malaria-causing-parasite/article5045356.ece>
- 6) Malaria Parasite-synthesized Heme is Essential in the Mosquito and Liver Stages and Complements Host Heme in the Blood Stages of Infection. Recommended in F1000 Microbiology for new finding and novel drug target. <http://f1000.com/prime/718071268>

Selected Invited Talks/webinars:

- 1) “Challenges in Malaria Elimination and Eradication” in Webinar for G-20 - Jan Bagidhari Program Webinar series on April 2023

- 2) “Malaria: Challenges Ahead in Diagnosis and Treatment” in Odisha Biotech Startup Summit 2022 on September 2022.
- 3) “Biosynthetic heme of Malaria Parasite and Cerebral Malaria” in Community Welfare Society Hospital, Rourkela, 12th March, 2021.
- 4) Nagaraj, V.A. 2019. Delivered an invited lecture on “Malaria Elimination and Eradication - A Serious Concern of Asymptomatic Malaria”, in 30th National Congress of Parasitology & Global Summit on Malaria Elimination held at JNU, New Delhi, 26th-28th September, 2019.
- 5) “Malaria Diagnosis - Need for Ultra-sensitive Diagnostics” in the symposium “Emerging Trends in Biological Sciences and Research” organized by Institute of Life Sciences, Bhubaneswar, 18th-19th March, 2019.
- 6) Invited lecture on “Malaria Elimination and Eradication - Quest for Transmission Intervention Strategies” in “14th International Conference on Vectors and Vector Borne Diseases” organized by Regional Medical Research Centre, Bhubaneswar, and National Academy of Vector Borne Diseases (NAVBD), 9th-11th January, 2019.
- 7) “Heme Dynamics in Malaria Parasite” in “International Symposium on Malaria Biology and 29th National Congress of Parasitology on Basic and Applied Aspects” organized by University of Hyderabad jointly with CCMB, CDFD, NIAB, TIFR (Hyderabad) and the Indian Society for Parasitology, 1st-3rd November, 2018.
- 8) “Malaria Parasite Biology - Molecular Mechanisms Underlying Disease Transmission” at Tata Institute for Genetics and Society (TIGS), Bangalore, on 26th July, 2018.

Awards and Recognitions:

- 1) Received National Academy of Vector Borne Diseases (NAVBD) Award for Outstanding Contribution on Molecular Biology from National Academy of Vector Borne Diseases, February 2017.
- 2) Global Health Travel Award funded by the Bill and Melinda Gates Foundation to attend Keystone Symposia on “The Science of Malaria Eradication” held at Mexico in February, 2014.
- 3) Awarded Ramanujan Fellowship for the year 2010 by Department of Science & Technology, Govt. of India.
- 4) Prof. Giri Memorial Medal, Institute of science, Bangalore for the Best Ph.D. Thesis of the year 2009-2010, Dept. of Biochemistry, Indian Institute of science, Bangalore.

- 5) Dr. A. S. Perumal Award, Indian Institute of science, Bangalore for the Best Performance in Research Training Program, Dept. of Biochemistry, Indian Institute of science, Bangalore.
- 6) Sathya Bhama Award, JIPMER, Pondicherry University for the Best Outgoing Student (2003).
- 7) Best Outgoing Student Award (2000), Sri Sankara Arts and Science College, Madras University

Other Credentials:

Examiner of Ph.D. thesis:

- 1) Plasmodium liver stage biology: discerning host invasion and egress using reverse genetics - CDRI, Lucknow.
- 2) Study of Protein Neddylation in Malaria Parasites - CCMB, Hyderabad.
- 3) Identification and characterization of CRLs of malaria parasite - CCMB, Hyderabad.

Supervisor of Ph.D degree awarded/ thesis submitted:

- 1) Malaria parasite heme biosynthesis regulates hemozoin formation, food vacuole integrity and cerebral pathogenesis - ILS, Bhubaneswar.
- 2) Distinct Evolution of Plasmodium Glutamine Synthetase with Species-specific Essentiality and its Implication in Artemisinin Resistance - ILS, Bhubaneswar.
- 3) Plasmodium berghei amino acid transporter 1 localized in the food vacuole is associated with cerebral pathogenesis in mice - ILS, Bhubaneswar.

Reviewer of Journals:

Nature Communications, International Journal for Parasitology, Scientific Reports, Journal of Bacteriology & Parasitology, Molecular Biotechnology, Experimental Parasitology & Infection and Immunity

Membership in Societies

Life Member in Society of Biological Chemists (India) and Molecular Immunology Forum (India).

Research Projects:

S. No.	Title of Project	Source of Funds	Duration
1	Griseofulvin as an adjunct drug for the treatment of cerebral and severe malaria (Formally approved)	BIRAC	2023-2024
2	Evaluation of safety and efficacy of curcumin (Biocurcimax capsule) as an adjunct drug to standard therapy [(Artesunate) + (Sulfadoxine-Pyrimethamine) tablet] for treatment of uncomplicated P. falciparum malaria. Phase-IIa Double-blind Clinical Trial. BT/PR32309/TRM/120/250/2019.	DBT	2020-2024
3	Screening of Plant Extracts from North East for Identifying Phytochemicals with Potent Antimalarial Activity against Asexual, Sexual and Liver stages of Malaria Parasite. (In collaboration with IBSD, Imphal). BT/PR25214/NER/95/1078/2017.	DBT	2019-2023
4	Amino acid requirements in the sexual and liver stages of malaria parasite – An immutable and versatile target for malaria transmission. EMR/2016/005664.	SERB	2018-2021
5	Malaria Parasite Biology - An Avenue to Discover New Drug Targets. (In Collaboration with IISc & JNCASR). BT/PR13760/COE/34/42/2015.	DBT	2016-2022
6	An Innovative Algorithm-Based Detection of Identical Multi-Repeat Sequences (IMRS) in the Genome of Plasmodium and its Validation in Malaria Diagnostics. BIRAC. (In collaboration with Jigsaw Biosolutions, Bangalore). BIRAC-BT/SBIRI-1167/SBIRI-22/13.	BIRAC	2014-2016
7	Generation of Prototype Lateral Flow Assay Kit using Antigen Specific Hybridomas to Develop Rapid Diagnostic Test for Clinical Diagnosis of Malaria. (In collaboration with Indian Immunologicals, Hyderabad)	BIRAC	2012-2015
8	Deciphering the Functional Significance of Rab-	DST	2012-

	mediated Vesicular Trafficking Processes in Malaria Parasite. SR/FT/LS-116/2011.		2015
9	Exploring the New Facets of Plasmodium Biology to Identify Potential Drug Targets. Ramanujan Fellowship. SR/S2/RJN-13/2010.	SERB	2010-2015