भारतीय विज्ञान शिक्षा एवं अनुसंधान संस्थान पुणे
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5th August 2023.

**This is to certify that the research work under reference is very recent and has not been given any award in the past.**

Dr. Siddhesh S. Kamat has made original and significant contributions in the field of functional annotation of uncharacterized enzymes and biological pathways, particularly lipid signaling and metabolic pathways associated with human neurological, immunological and metabolic disorders. Further, his lab has developed cutting-edge LC-MS/MS-based lipidomics and metabolomics techniques, which have lead to identification and quantification of important biological molecules, that have significant implications in various human diseases and infections.

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Paper # 1: Khandelwal, N., Shaikh, M., Mhetre, A., Singh, S., Sajeevan, T., Joshi, A., Balaji, K. N., Chakrapani, H., **Kamat, S. S.*** (2021) Fatty acid chain length drives lysophosphatidylserine dependent immunological outputs, ***Cell Chemical Biology*** 28, 1169-1179.
*Article featured on August 2021 issue cover of Cell Chemical Biology.*

Following up on his lab's discovery of ABHD12's lipase activity, and its association to the human neurological disorder PHARC via modulation of immunomodulatory lysophoshatidylserine (lyso-PS) and pro-apoptotic oxidized phosphatidylserine lipids (Kelkar et al., *Nature Chemical Biology, 2019*), his lab has reported the first successful synthesis of the lyso-PS lipids, and using these, they have shown that as a function of the lipid tail length, these hormone like signalling lipids act through TLRs to elicit pro-inflammatory responses to cause neuroinflammation or via GPCRs to cause activation of macrophages and histamine release from mast cells (**Khandelwal et al., *Cell Chemical Biology, 2021***). This study has paved the wave for the development of bioorthogonal lyso-PS lipids, that can now be used to map the protein ligands for this biomedically important signalling lipid class, and for development of TLR2 antagonists as therapeutic targets in treating neuroinflammation and PHARC.

**Authors' contribution:** Siddhesh S. Kamat is the lead corresponding author and has conceptualized and supervised these studies, that were funded by a DBT/Wellcome Trust India Alliance grant to Siddhesh S. Kamat. The co-first authors are Postdocs and Ph.D. students of Siddhesh S. Kamat and the work done by the Ph.D students has been included in their respective dissertations. We collaborated with Prof. Harinath Chakrapani for the synthesis aspects of this project, and Prof. K. N. Balaji provided the TLR2 null mice used in this paper.

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Paper # 2: Mehdiratta, K., Singh, S., Sharma, S., Bhosale, R. S., Choudhary, R., Masal, D. P., Manocha, A., Dhamale, B. D., Khan, N., Vivekanand, A., Sharma, P., Ikeh, M., Brown A. C., Parish, T., Ojha, A., Michael, J. S., Faruq, M., Medigeshi, G. R., Mohanty, D., Reddy, D. S., Natarajan, V. T., **Kamat, S. S.***, Gokhale, R. S.* (2022) Kupyaphores are zinc homeostatic metallophores required for colonization of *Mycobacterium tuberculosis*, ***PNAS*** 119(8), e2110293119.

It has been known for many years that *Mycobacterium tuberculosis* (MTB) needs optimal concentrations of metals for survival under stressful conditions, however, that pathways and/or secondary metabolites that regulate this, remained unknown till recently. Using a combination of genetic models and stress conditions developed by Rajesh Gokhale' lab, and leveraging advanced lipidomics/metabolomics technologies, our lab identified a set of secondary metabolites, we termed "kupyaphores", that are able to regulate zinc homeostasis in MTB (***Mehdiratta et al., PNAS, 2022***). This study shows for the first time, a need for zinc by MTB, and uncovers a previously unknown zinc acquisition strategy by pathogenic microbes that can modulate host-pathogen interactions and disease outcomes.

**Authors' contribution:** Siddhesh S. Kamat is a lead/co-corresponding author with Rajesh Gokhale, and together, they conceptualized and supervised these studies. This study was funded in part by a DBT/Wellcome Trust India Alliance grant to Siddhesh S. Kamat. The second author is Ph.D. student of Siddhesh S. Kamat and the work done by the Ph.D students from Siddhesh's and Rajesh's labs has been included in their respective dissertations. All the LC-MS/MS work done in this paper, and the identification of the structures of the kupyaphores were done in the Siddhesh S. Kamat's lab using the LC-MS/MS-based metabolomics/lipidomics platforms developed by the lab at IISER Pune.

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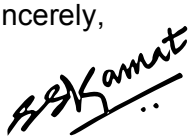
Sincerely,



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