National Centre for Biological Sciences (NCBS)
Tata Institute of Fundamental Research (TIFR)
(A unit of Department of Atomic Energy)
Government of India

Prof. LS Shashidhara FASc FNASc FNA
Centre Director

14 August 2024

The Chairperson
Sun Pharma Research Foundation Research Fellowships 2024
Pharmaceutical Sciences Category

Sub: Letter of Nomination for Dr. Siddhesh S. Kamat of IISER Pune, India

Dear Chairperson,

I am writing this nomination letter in strongest possible support of Dr. Siddhesh S. Kamat from IISER Pune, who is applying to the Sun Pharma Science Foundation Research Fellowships 2024 in the Pharmaceutical Sciences Category.

Research in Siddhesh's lab at IISER Pune focuses on studying the biological mechanisms of lipid signaling pathways in the mammalian physiology, and how dysregulation in this lipid metabolism results in human pathological conditions and diseases (e.g. neurodegenerative diseases, autoimmune diseases, metabolic syndrome, infections, inflammation etc.). Siddhesh's lab has a special interest in identifying and functionally characterizing hitherto unknown lipid signalling pathways, annotating the metabolic enzymes and cognate receptors that regulate their biology, and providing new mechanistic insights and therapeutic opportunities for treating human diseases. He has been credited for integrating diverse chemical biology approaches with cuttingedge liquid chromatography coupled to mass spectrometry (LC-MS) based lipidomics and metabolomics techniques towards achieving the aforementioned research goals. This innovative multi-pronged chemical biology strategy developed by his lab marks a paradigm shift in how chemical biologists' worldwide study such poorly abundant, under-studied, yet physiologically important, signalling lipids *in vivo* in humans.

Specifically, Siddhesh's lab has made seminal contributions in understanding the array of signalling pathways associated with the lysophosphatidylserine (lyso-PS) class of lipids. His lab has identified and biochemically characterized the lipases that biosynthesize or degrade this signalling lipid, developed synthetic protocols to make lyso-PS chemically, and using these mapped different receptors for these lipids in the mammalian central nervous and immune systems (*J. Biol. Chem.* 2018; *Nature Chem. Biol.* 2019; *Biochemistry* 2020; *Cell Chem. Biol.* 2021; *E. J. Neurosci*. 2021). The research from Siddhesh's lab on lyso-PS lipids has contributed to the understanding of the molecular basis of (neuro)inflammation, and neurodegenerative disorders such as PHARC, Complex HSP, and newer biologically targets are being investigated clinically to treat these genetic diseases. Given their contribution in understanding the biology and pharmacology of lyso-PS lipids, his lab recently (in April 2024) published a comprehensive, authoritative and critical review of this topic, in the prestigious ***Chemical Reviews*** journal (Journal Impact Factor: 51.4).

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Besides lyso-PS lipids, his lab has also deciphered previously unknown lipid signalling pathways during diverse immunological processes like phagocytosis, ferroptosis, and bacterial infections (*ACS Chem. Biol*. 2018; *J. Med. Chem*. 2019; *ACS Chem. Biol*. 2021; *Microbiol. Spectrum* 2023). Lastly, his lab has annotated the enzyme ABHD14B as a novel lysine deacetylase, and shown its role in systemic glucose metabolism, diabetes and metabolic syndrome (*Biochemistry* 2020; *J. Biol. Chem*. 2022, *Proteins* 2023).

Uniquely and very importantly, from a technological and applications standpoint, his lab has established state-of-the-art LC-MS facilities that cater to numerous advanced lipidomics and metabolomics platforms to facilitate and unravel novel mechanisms associated with onset and progression of diseases caused by perturbed lipid homeostasis. These LC-MS based lipidomics and metabolomics platforms developed in his lab are unique to any research group within India, and his lab is perhaps the only one within the country capable of doing the aforementioned studies at the highest global standard. From a pharmaceutical or biotechnological applications stand point, these lipidomics/metabolomics platforms are now emerging as key technologies in identifying dysregulated molecular pathways in diverse human diseases, and enabling development of new therapies against them.

Since joining the Department of Biology at IISER Pune in 2016 as an Assistant Professor, Siddhesh has established himself as a globally competitive chemical biologist and lipid biochemist, and published numerous high-quality publications in reputed journals such as *Nature Chemical Biology*, *Cell Chemical Biology*, *PNAS*, *ACS Chemical Biology, J. Biological Chemistry etc*. In addition, his lab has extensively collaborated with several researchers within the country, and often enabled them to reveal underlying metabolome-dependent phenotypes across scales and model systems. These collaborations have also yielded high quality papers in various domains on biological sciences in reputed journals like *PNAS*, *Elife*, *J. Cell Biology, mBio, Chemical Science, etc.*. Additionally has lab has also published several comprehensive reviews in reputed journals such as *Chemical Reviews*, *Biochem. Soc. Trans.*, *RSC Chem. Biol*., *Curr. Opin. Chem. Biol*., etc.

Considering his unique expertise, his lab is highly sought after by many top-notch scientists in India and from around the world for help in the fields of LC-MS based lipidomics, lipid metabolism and signaling. While providing such help selflessly, he has not lost focus on his primary research, as evident from his lab's publication record over these years. Given his excellent academic track record, in 2020, Siddhesh was promoted to an Associate Professor within 3.5 years of joining IISER Pune, something that is rare in Indian academia. Additionally, given his track record, Siddhesh is a recipient of numerous reputed awards, such as the SwarnaJayanti Fellowship (2021), CDRI Award for Excellence in Drug Research (2021), EMBO Young Investigator Award (2020), Merck Young Scientist Award (2019), INSA Young Scientist Medal (2019), DBT/Wellcome Trust India Alliance Intermediate Fellowship (2016) to list a few. Of note, Siddhesh is one of only 4 Indian scientists to receive the prestigious and highly coveted EMBO Young Investigator Award, and the only Indian to do so in 2020, from a cohort of 27 scientists globally chosen for this award.

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Finally, given his expertise in the fields of lipidomics, lipid metabolism, chemical biology and pharmacology, Siddhesh is on the Editorial Board of two prestigious society journals namely, *British Journal of Pharmacology* and *J. Biological Chemistry*, all of which are testament of recognition of his lab's high-quality research by the global community at very high standards.

The Sun Pharma Foundation Research Fellowships 2024 in Pharmaceutical Sciences category recognises achievements in the identification of new drug targets and Siddhesh's research program at IISER Pune has made several very significant contributions to this field, both in terms of biological discoveries and development of LC-MS based technologies towards studying them. Therefore, given his academic credentials, area of research, and the eligibility criteria for this award, I feel that Siddhesh would be an ideal candidate and strongly recommend his application for this year's Sun Pharma Foundation Research Fellowship in the Pharmaceutical Sciences Category.

Best wishes,

LS Shashidhara