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To,

August 15th, 2024

Prof. Virander S. Chauhan
Chairman, Sun Pharma Science Foundation

Subject: Nominating Shirsha Saha for the Sun Pharma Science Scholar Fellowship, 2024

Dear Prof. Chauhan,

I am absolutely delighted to write this letter of support towards Ms. Shirsha Saha's application for the Sun Pharma Science Scholar Fellowship, 2024. Shirsha is a truly phenomenal graduate student in my laboratory at the Indian Institute of Technology, Kanpur, India, and she has made outstanding contributions on the structure and function of selected G protein-coupled receptors (GPCRs) during her Ph.D.

Shirsha has focused primarily on the structure and function of the human Duffy antigen receptor for chemokines, an enigmatic seven transmembrane receptor that lacks canonical transducer-coupling and downstream signaling pathways, unlike prototypical GPCRs. This receptor serves as one of the most promiscuous chemokine binding protein in our immune system, and also the primary anchor site for the malarial parasite, *Plasmodium vivax*, as well as for the pore forming toxins secreted by *Staphylococcus aureus*. Shirsha combined biochemical, cellular, pharmacological, and structural approaches, to illuminate the intricate details of ligand-recognition, activation, functional divergence, and potential non-canonical signaling pathways downstream of this intriguing receptor. This is truly a pathbreaking discovery representing an area that was being pursued by multiple laboratories across the globe, and her findings were recently published in Cell (2024). Shirsha has also spearheaded parallel projects on the structure and function of the complement anaphylatoxin receptors and chemokine receptors, with an emphasis on deciphering their activation, signaling, and regulatory mechanisms. Her efforts on the complement anaphylatoxin receptors were truly monumental, leading to publication of the findings in Cell (2023), and Shirsha is one of the lead authors on the study. Shirsha's ongoing efforts on the structure, function, and atypical dimerization of the chemokine receptors have yielded several unanticipated and exciting findings with broad implications for the paradigms of GPCR activation and signaling, and the findings have been favorably reviewed in high visibility outlets and are expected to be published soon.

Taken together, Shirsha's research has revealed fundamental insights into structure, function and signaling of selected chemo-attractant receptors with direct implications for novel drug discovery. Shirsha has emerged as a poster child of the Ph.D. program in our department at IIT Kanpur with truly exceptional performance, and she is poised to emerge as an outstanding leader and scientist in the coming years. Her team spirit, communication skills, guidance to the new entrants in the laboratory, and leadership have all been truly remarkable and exemplary, and therefore, it has been a privilege for me as a mentor to host her in our laboratory over the past several years.

Shirsha is the most deserving candidate for the Sun Pharma Science Scholar Fellowship in Biomedical Sciences, and I nominate her with my highest possible recommendation. I sincerely hope that the committee decides favorably on her candidature. Please feel free to contact me for any additional information.

Sincerely,

Arun Kumar Shukla