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Dear Members of the selection committee,
Sun Pharma Science Foundation Science Scholar Fellowship,

It is my great pleasure to write this letter for Mr. Sreepadmanabh M nominating him for the Sun Pharma Science Foundation Science Scholar Fellowship. Sreepadmanabh—commonly known as Sree— is a 4th year Ph.D. student at NCBS and is interested in understanding cell biology in 3D cell culture and artificial tissues. More specifically, he is interested in how cells grow in 3D, respond to external stimuli, and transport small molecules. Sree certainly belongs to the top 1% of graduate students that I have encountered throughout my career at the University of Florida, Princeton University, and NCBS. There is no doubt that Sree is the best student that I have encountered at NCBS. Before joining NCBS, he had published one research paper and two review papers in very prestigious jounrnals.

For his first project, Sree has designed a high throughput and innovative method to create a 3D cell growth medium. Sree used falshsolidification of molten agar directly inside cold cell growth media to make agar microgels—a concept from material science research—which were then centrifuged to create a 3D matrix where cells can be easily placed using the current understaning of jammed systems in soft matter physics. This 3D cell growth medium is extremely versatile and can support the growth of a wide range of prokaryotes and eukaryotes due to its neutral nature. The extremely transparent nature of these matrices allow us to directly visualize cellular behavior in 3D. Furthermore, this platform is directly used for freeform embedded 3D printing wich allows us to directly pattern cells inside a 3D cell growth media.

Next, using such a 3D culture system that recreates the structural and viscoelastic properties of gut mucus, Sree has pioneered a technique for understanding bacterial growth in a mucus-like environment—how altering the physical properties of their microenvironment influences bacterial growth under confinement. Sree reported that low aspect-ratio bacteria form compact, spherical colonies under confinement while high aspect-ratio bacteria push their progenies further outwards to create elongated colonies with a higher surface area, enabling increased access to nutrients. As a result, the population level growth of high aspect-ratio bacteria is more robust to increased physical confinement compared to that of low aspect-ratio bacteria. His work is exemplary as it captures the first ever evidence that physical constraints play a selective role in bacterial growth based on cell shape. His work will directly impact how we think about antibiotic resistance, bacterial ecology and evolution inside complex environments mimicking their natural niches. Currently, Sree is collaborating with Dr. deepa Agashe's lab exloring how bacteria evolve in3D complex environments and with Dr. Amey Redkar's lab at NCBS to visualize the plant fungal interaction inside a transparent 3D soil like environment.

Finally, a fundamental question in biology is how mammalian cells integrate and respond to manifold environmental cues 3D. Oxygen availability and ECM properties are two of the most prevalent, yet dramatically varying microenvironmental cues across most physiological settings. Sree has addressed this question by subjecting cells to a combination of oxygen partial pressures and ECM densities - an oxo-mechanical cue - and investigated their 3D morphology at the single cell level. Combining morphometric measurements, bulk transcriptome analyses, as well as chemical modulation of

intracellular mechanics and oxygen-driven signalling, Sree has established a set of phase spaces that define cellular behavior across different oxo-mechanical regimes. He has showen that a cell's response to varying oxygen availability depends on both substrate and intracellular mechanics; while the cell's engagement with mechanically diverse substrates is influenced by oxygen-driven signalling processes. His work identifies—for the first time—an oxo-mechanical regulation of cellular behavior in 3D. He is currently in process of submitting this paper.

Sree is an exceptionally driven and self-motivated young scientist. His passion and innovative thinking for biological sciences is unparalleled. Being the first graduate student of my lab, he has single-handedly set up most of our current experiments, designed their protocols, and trained new joiners. He has worked in our lab for the past three years and during this period, he has already published two papers and one paper is under review. He is an amazing mentor. He has mentored several summer interns and one MS thesis student till today. The MS thesis student has coauthored two reseach papers with him. Sree is a very good orator. He has received the best poster award for his Ph.D. research at four different national conferences. In March 2024, he was awarded the Distinguished Student Program Award by the American Physical Society at Minneapolis, USA. This is a highly competitive award and is given to less than 10 graduate students in the world every year. Sree received this prestigious award based on his work over the last two years.

Sree has huge potential to do more amazing science in the near future. All of his projects are pioneering in nature. They have opened new direction in our lab and helped us to design new reseach directions. His capability of writing new reseach proposal is unparalled. He has contributed in several research proposal that we have submitted. Sree aims become an independent scientist and start his own lab in future. Sun Pharma Science Foundation Science Scholar Fellowship will inspire and encourage him to pursue his dream. I would wholeheartedly recommend Sree for this award. I would be happy to provide any further information if needed.

Yours sincerely,

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