



Biosketch

Darshan Trivedi, PhD (biochemistry/biophysics/physiology)

Dr. Darshan Trivedi is a Life Science Research Scientist in the Department of Biochemistry at Stanford University. He received his B.S. in biotechnology (2005) and M.S. in biochemistry (2007) from India. He then earned his PhD in Physiology (2014) Pennsylvania State University. In 2015, he joined the laboratory of Dr. James Spudich at Stanford as a Postdoctoral Fellow and was subsequently promoted to a Life Science Research Scientist in 2019.

Dr. Trivedi's research for his M.S. degree was on the structural and functional analysis of the protein ubiquitin. This was where he realized the immense potential of interdisciplinary research of biophysics and biochemistry, leading him to join a lab working on the biochemistry of myosin motors for his PhD research. Dr. Trivedi has spent more than a decade understanding the biochemistry and biophysics of myosin motors. For his PhD work at Pennsylvania State University, he studied the mechanism by which the unconventional myosin, myosin V, transduces chemical energy into force production. Dr. Trivedi used myosin V as a model system to map communication pathways in this highly allosteric molecule using fluorescence spectroscopy, transient kinetics, and other biophysical tools.

For his thesis project, Dr. Trivedi was awarded a two-year prestigious American Heart Association Pre-doctoral Fellowship. Dr. Trivedi has six important publications and two invited book chapters from his graduate research work on myosin motors. His PhD work resulted in 14 poster/oral presentations at various conferences, including the Annual Biophysical Society Meetings where he has consistently presented his work as a lead author since 2009. He has also presented his work as an invited oral session and as a poster at two Gordon Research Conferences.

In addition, Dr. Trivedi has received numerous awards and fellowships as part of his graduate career. He received the prestigious Student Research Achievement Award from the Biophysical Society for his graduate work, several awards from the Pennsylvania State University including an Alumni Endowed Scholarship, and an award for outstanding performance by a PhD candidate. Notably, he received an endowed Graduate Fellowship as an outstanding recruit to the Pennsylvania State University Physiology program.

Dr. Trivedi was also selected as a student representative to be part of a scientific task force to address challenges in scientific funding. He represented the academic setup and met with Senators and Representatives at the Pennsylvania Capitol.

For his postdoctoral work, Dr. Trivedi continued his quest to understand myosin motors, now pivoting to applied research and focusing on the clinically relevant human beta cardiac myosin. His work led to two significant breakthroughs in understanding and treating hypertrophic cardiomyopathy (HCM). Soon after joining the Spudich lab, his work elucidated the molecular mechanism of cardiac hypercontractility typically seen in patients with HCM. His work uncovered a critical, energy-conserving off-state of the beta cardiac myosin which is disrupted when HCM-causing mutations occur in the myosin molecule. These mutations cause myosin to adopt more of an on-state which constitutively generates force even when it is not required. This work

opened an arena of novel research to therapeutically target this energy conserving state of myosin molecule in the heart to develop targeted inhibitors and activators.

Appropriately, his follow-up work included uncovering the mechanism of action of mavacamten, a small molecule cardiac inhibitor currently in phase III clinical trials by MyoKardia to treat HCM. Dr. Trivedi along with a team of researchers from two companies and four academic institutions discovered that at the molecular level, mavacamten shifts the equilibrium of the 'on-and off-state' myosin motors, causing the mutated, constitutively 'on' myosin motors to adopt more of an 'off-state'. This leads to a reduction in contractility of the hypercontractile heart.

As a postdoctoral fellow, Dr. Trivedi has published seven manuscripts since 2015. He has received multiple research fellowships including a Postdoctoral Fellowship from the Lucile Packard Children Health Research Institute at Stanford University, and a two-year American Heart Association Postdoctoral Fellowship.

Dr. Trivedi has presented his postdoctoral research at multiple scientific forums. He was also selected to attend an intensive workshop on "Managing Science in the Biotechnology Industry" organized by the American Society for Cell Biology. Dr. Trivedi has received several awards during his tenure as a postdoctoral fellow at Stanford. Notably, he received the "Outstanding Research Award" twice at the Stanford Drug Discovery Symposium in 2016 and 2018, was awarded the "Best Manuscript Award" from the Cardiovascular Institute at Stanford University in 2019 for his work on mavacamten, and also received a Young Investigator Award by the European Muscle Society in Budapest, Hungary in 2018.

Besides research, Dr. Trivedi has actively assumed leadership and membership roles in several professional and social organizations. He served as a Founding President for Association of Indians at Hershey, an organization in Pennsylvania State University raising funds to support social development and community projects in the US and India. He was on Pennsylvania State University's Dean's Council on Diversity, and a recipient of the Diversity Champions Award for fostering cultural diversity education on campus. Most recently he was an organizing member of the Association of Industry-Minded Stanford Professionals, and continues to be actively involved as a volunteer and project co-manager for the Association for India's Development, a non-profit organization working on social projects pertaining to, education, healthcare, women empowerment, social justice, and natural resources conservation in India.