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Biosketch

Suman Nag, PhD in biochemistry/biophysics

Suman Nag, Senior Scientist at MyoKardia Inc.,received his B.S. in chemistry from Calcutta University, India in 2004 and his MS-Ph.D. in biophysics from Tata Institute of Fundamental Research (TIFR) in 2011. From 2011 to 2016 he did postdoctoral work in the Department ofBiochemistry at StanfordUniversity with Dr. James Spudich.He thenserved asa Senior Scientist in the Department of Protein Sciences at Merck for a year and a half. He was then recruited to MyoKardia as a Scientist-II in 2017 where he has been leading the biochemistry and biophysics team and has recently risen to the position of Senior Scientist-I to develop and lead a sarcomere biology group.

Duringhis postdoctoral work in the Spudich lab, he wasdeeply involvedin understanding the molecular basis of hypertrophic cardiomyopathy, a genetic disease that affects 1 out of 500 individuals and leads to sudden death. In his tenure, he co-led different studies in understanding two different missense mutations in human cardiac myosin: one which increases the intrinsic force production of myosin (R453C) and the other which impairs velocity of contraction (R403Q). These works directly laid the initial hypothesis behind the formation of MyoKardia in 2012.Currently, two different molecules from MyoKardia are in clinical trials: a cardiac inhibitor (mavacamten) in phase III and a cardiac activator (MYK-491) in phase II. Both of these molecules hold great promise for small molecule therapeutic intervention for different categories of heart failure. These two therapeutics are based directly on Nag's contribution to the Spudich laboratory.

Nag's research on sarcomere biology continues at MyoKardia where he is devoted to the understanding of the molecular mechanism of actions of many effector molecules, including mavacamten and MYK-491, which target the myosin and the regulated actin system. The biochemical understanding generated by Nag and his colleagues has helped MyoKardia put forward two more pre-clinical programs in the pipeline.From his earlierbiochemical studies done at Stanford using different reconstituted domains of the myosin molecule, he along with his team mates were the first to experimentally provide strong evidence for the 'myosin-mesa' hypothesis and showed that single-point HCM mutations in specific myosin domains disrupt the equilibrium from a sequestered 'OFF-state' of myosin heads to their 'ON-state', leading to the clinically observed hypercontractility. Later, this study combined with follow-up studiesin the Spudich laboratory showed that this structural 'OFF-state' of myosin is a super-relaxed state (SRX), and that mavacamten acts by converting myosin from an open state to this SRX state. At MyoKardia, other than understanding MoAs of pipeline molecules, Nag is heavily invested in basic sarcomeric research and is focused on developing new technologies. Currently, he is collaborating with the Argonne National Lab facility and ISS on two separate projects to understand cardiac muscle system better at a molecular level.

Earlier during his Ph.D., Nag was involved in understanding protein misfolding and aggregation of amyloid-beta and alpha-synuclein proteins, which play a significant role in the progression of Alzheimer's and Parkinson's disease. During his work, he discovered how a critical misfolding event that occurs in the early stage of protein folding could lead to toxic oligomer formation ofthese proteinsand subsequently lead to the associated neurological disorders. During his Ph.D., Nag was on a six months sabbatical to work at Purdue University as a Visiting Scholar, on a project related to the Toll-like receptor 9 (TLR9) activation of the innate immune system. Years later, Nag utilized his protein misfolding and immunology knowledge in a completely independent study at Merck, where he had the principal leadership role in the physio-chemical and biophysical characterization of various monoclonal antibodies, bispecific antibodies, and nanobodies as novel molecules for differentimmuno-oncological targets. In parallel Nag also led a team to develop innovative and efficient developability platforms to screen for a biologics drug candidate, using their thermal, colloidal, and structural properties. His research eventually helped in pushing one antibody and one nanobody into the pipeline as pre-clinical check-point inhibitors.

Nag has published numerous important biophysics papers, with over 750 citations, dealing with molecular mechanisms of hypertrophic cardiomyopathy, development of Alzheimer's disease and work on serotonin and dopamine-mediated neuronalsignaling associated with mood regulation and depression. Nag has presented his work and has been an invited speaker at the Gordon Research Conference on 'The Molecular Motors' andthe 'Asian Represent Conference' at Harvard Medical School. He has given seminars on 'Bridging the Gap between Academia and Industry'at the University of Vienna, TIFR, Mumbai, and TIFR, Hyderabad. Since 2016 Nag has also been a guest lecturer at Stanford University teaching 'Genetic Diversity and Personalized Medicine'. Nag currently serves as a member of the South Asian Heart Association (SAHA), a part of the Red Saree,for raising cardiovascular health awareness amongst South Asian communities in the US. In 2007, Nag co-foundedUMEED, a non-profit organization dedicated for socio-economic causes and natural calamity relief work in the rural areas of India.

Nag has received numerous awards. For his undergraduate work in 2004, he was awarded the prestigious 'TIFR Graduate Scholarship' and the 'KanwalRekhi Scholarship'. As a student of biophysics, Nag was awarded the 'International Student Award' by the Biophysical Society in 2008 followed by the'Government of India Student Award' by the Center for Cooperation in Science and Technology among Developing Societies (CCSTDS), Ministry of Science and Technology and Department of Science and Technology (DST) in 2009. In 2010, Nag was awarded the 'Company of Biologist Student Award, UK' and the 'Government of India Student Award' by the Council of Scientific and Industrial Research (CSIR), Human Resource Development Group. In 2012, Nag was given the 'Zita-Lobo' honorable mention best thesis award. Later that year Nag secured the Stanford Dean's fellowship to carry out his postdoctoral research in the Spudich lab. In the industry biosphere, Nag was awarded three different 'Awards of Excellence' in 2016 by Merck for helping the team push two different biologics molecules to the preclinical pipeline, and two different 'Pulse Silver Technical Innovation Awards' in 2018 by MyoKardia for technical innovation to understand small-molecule mechanisms of action on sarcomeric proteins.