

**Statement of research achievements, if any, on which any Fellowship has already been received by the applicant.**

During my postdoctoral tenure at University of Massachusetts Medical School, USA, I was honoured with the prestigious **American Heart Association (AHA)** post-doctoral fellowship.

The title of the research proposal was “Cryo-EM structure of the inhibited form of cardiac myosin and its relation to hypertrophic cardiomyopathy”. This groundbreaking research aims to determine the atomic structure of beta-cardiac myosin in its inhibited state, a feat that has not been achieved before. I drew inspiration from our Nature paper, where we solved the near-atomic structure of smooth muscle myosin to learn how to preserve the beta-cardiac myosin in its inhibited state, which is also a shut-down state of myosin.

To start with a general overview, the human heart is an essential organ that pumps blood to different body parts. It is made from a special type of muscle (cardiac muscle), which makes our heart keep working our entire life and never stop till death.

Sometimes, our heart suffers from genetic diseases, such as HCM, where the heart muscle becomes thicker, making it harder to pump blood. This can cause shortness of breath, chest pain, and abnormal heart rhythms, which in some cases lead to sudden death. Heart muscle is made up of several proteins. An important one, called myosin, forms filaments that slide along the other major protein filaments made of actin, causing the muscle to contract.

Myosin, with its two heads and a long tail, plays a pivotal role in cardiac relaxation, which occurs at the end of every heartbeat. In HCM, the myosin heads show defects in their interaction. We need to know the molecular details of these interactions to understand these defects and how cardiac muscle relaxes normally. Using the Cryo-electron microscopy technique, the proposal was to determine the structure and interactions at the molecular level. This state-of-the-art technique is ideally suited to study large protein complexes like myosin. The information we gather will deepen our understanding of HCM at the molecular level and pave the way for potential future treatments by therapeutic drugs, offering hope and optimism to those affected by this condition.

The AHA fellowship was started in Jan 2022, and after six months, I accepted the position as an assistant professor at the Indian Institute of Technology (IIT) Roorkee. I could complete only the preliminary sample optimisation and negative staining.