Roop Mallik: From machines to molecular motors

Kimberly Siletti

Roop Mallik studies how molecular motors and lipids interact to drive intracellular transport.

A physicist by training, Roop Mallik has always been fascinated by machines. In school he would visit his father's machine shop to watch the equipment whir and creak and produce a result he could never guess beforehand. The experience instilled in him a keen interest in building instruments.

Mallik decided to pursue an undergraduate degree in physics at the university in Allahabad, a city in northern India on the banks of the Ganges River, where he was raised. He then completed a PhD in physics, studying heavy fermion magnetism with E.V. Sampathkumaran at the Tata Institute of Fundamental Research (TIFR) in Mumbai, India. TIFR provided an environment where Mallik could interact frequently with biologists and chemists. These interactions gradually opened his mind to possibilities outside physics. Mallik realized that his background in physics and instrument building could be used to observe biological phenomena on a molecular scale.

He decided to transition from physics to biology, first completing a short postdoc in chemistry at TIFR with G. Krishnamoorthy and then a longer one with Steven Gross at the University of California, Irvine. It was with Gross that Mallik first investigated the molecular motors, such as dynein, that are responsible for intracellular transport. Mallik is now trying to understand how motors interact with lipids as an associate professor at TIFR in the department of biological sciences. We contacted him to learn more.

What interested you about your current area of study?

Like everyone else, I grew up reading things such as, "Electrons move in orbits around the nucleus." However, there was no way to see this happening. The fact that you could actually see motor-driven cargoes moving around blew my mind. The idea that I could build an instrument (an optical trap) to measure the forces from motors as they tug cargo along . . . that was the icing on the cake.

What are you currently working on? What is up next for you?

Motors spend their lives pulling against lipid membranes in the cell, yet we know remarkably little about what the membrane and the motor mean to each other. In this context, we are focusing on phagosome maturation. Micrometer-sized particles (e.g., bacteria and parasites) are ingested by immune cells and enclosed within a lipid membrane to make a phagosome. Phagosome maturation is intimately connected to the spatiotemporal location of the phagosome inside cells. Motors carry the phagosome around so that it can interact with other organelles to exchange lipids and proteins by kiss-and-run fusion. These interactions ensure a phagosome's maturation and eventual fusion of its contents with lysosomes.

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We recently showed that the dynein motor undergoes geometrical reorganization to cluster into cholesterol-rich lipid rafts on the membrane of a maturing phagosome (1). This reorganization propels the phagosome toward degradative lysosomes by allowing many dyneins to generate collective force together against a microtubule. This is exciting because many pathogens survive by "hijacking" lipid rafts (2). Indeed we showed that *Leishmania* actually uses a glycolipid called lipophosphoglycans to disrupt the clustering of dynein into lipid rafts, thereby blocking transport of phagosomes toward lysosomes (1). These investigations followed up on an earlier realization that dynein's single-molecule architecture specially adapts it to work well in a team (3, 4, 5).

In the long run, I am also very interested to understand how motors control secretion of lipoproteins (VLDL) from the liver and if this is dependent on the feeding/fasting state of the animal (6). We are developing a hypothesis about how metabolic signals control motor-driven transport of lipid droplets and their consequent interactions with other organelles inside hepatocytes.

Roop Mallik. IMAGE COURTESY OF ROOP MALLIK.

What kind of approach do you bring to your work?

I always visualize a cellular process as a series of events happening at distinct time points and locations inside the cell. When building a hypothesis, the molecules are less important to me. I always worry more about geometry and causality. This is a pleasant hangover from my earlier life as a physicist. I wonder if traditional cell biologists think similarly. I have never asked them.

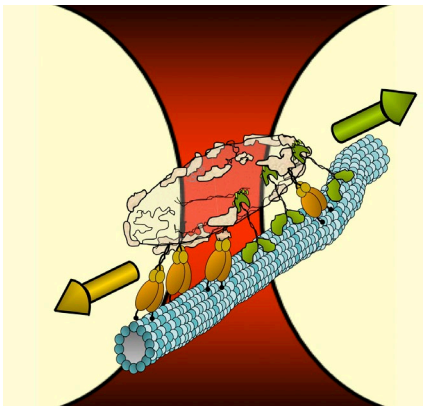
What did you learn during your PhD and postdoctoral research that helped prepare you for being a group leader?

To value diversity: diversity of approaches to a problem, diversity in the people who make up a laboratory, how they think, how they react to a situation, etc. This is one reason I returned to India to set up my laboratory. There is a larger standard deviation associated with everything here. I like it.

What has been the biggest accomplishment in your career so far?

My biggest accomplishment is a laboratory where my colleagues want to get to work every morning. They argue passionately about what they do, defend it with zeal, and are upset when things don't work. I do not ask for anything more.

ksiletti@rockefeller.edu



Cartoon of dynein and kinesin transporting an endosome in an optical trap.

Who were your key influences early in your career?

My mother, who carried on working very hard in spite of physical disability. She taught me not to complain. E.V. Sampathkumaran, from whom I learned the importance of building trust with my students. G. Krishnamoorthy, who guided me when I transitioned into biology. Steve Gross, from whom I learned to ask real biological questions and not just pretend to do biology as a physicist. My wife and colleague, Sreelaja, who was there to help when I didn't know how a protein was different from DNA.

What is the best advice you have been given?

Judge when a project is not working, and stop it if you have to.

What hobbies do you have?

I often go hiking solo to remote mountains and fortresses. These abandoned places fascinate me because here I can imagine events, ways of living, and people who are long gone. I also love sports and play regularly (table tennis and badminton).

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What do you think you would be if you were not a scientist?

I always wanted to be a waiter in a restaurant because I imagined that I could gorge on the food at my lunch break. I also wanted to be a veterinary doctor, because I am very inspired by the writings of James Herriot.

What has been your biggest accomplishment outside of the laboratory?

I wrote a script and directed a few plays when I was in college. I cannot think of anything more difficult than that one.

Any tips for a successful research career?

To quote William McFee, "The world belongs to the enthusiast who keeps cool."

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The Mallik lab at Marine Drive, Mumbai.