Published April 1, 2013

People & Ideas

Sandhya Koushika: Building new models and communities

Koushika studies axonal transport primarily in the worm *C.elegans*.

Efficient neuronal function depends both on the cell's ability to traffic proteins and organelles from the soma to the synapse and on the retrieval of endocytosed materials and other chemicals from those distant sites. Sandhya Koushika is intent on gaining a better understanding of the processes that govern axonal transport and how they are regulated during organismal development.

With a solid background in genetics (1) and in the neurobiology of *C. elegans* (2), Koushika spent the early part of her career developing techniques to study axonal transport in the worm (3, 4). Now, by combining the power of *C. elegans* genetics with these technologies, Koushika is already making new discoveries about axonal transport (5). She's also serving as an example for the burgeoning scientific community in her native India. We called her at her new lab at the Tata Institute of Fundamental Research in Mumbai to hear about her career so far and her plans for the future.

EARLY INSPIRATIONS

Do you recall any of your childhood interests?

I was a reader. I read all the time. And when I was very young, I became interested in doing research. If you were to ask me why, I couldn't give you an intelligent answer. I think I just thought a research career was the most fascinating thing in the whole world, without knowing anything about it. I remember reading about Marie Curie and seeing the tremendous progress she made and how dedicated she was, no matter what the difficulty; that was very eye-opening for me.

When my mother found out that this was what I was interested in, she actually encouraged me because she thought it would give me an opportunity to have a very balanced life with enough time to raise a family. I'm in the middle of moving my lab from Bangalore to Mumbai, so my life now could not be more different from what she probably imagined. But as I said, I was lucky that she and my father were very supportive of my interests, and they also let this be known amongst their friends. People would make photocopies of *Scientific American* articles and send them to me to read.

So you didn't personally know any researchers…

No. I grew up in a small town in Gujarat, so I didn't know any people who did research as their career. Nonetheless, I think it was expected that I would pursue higher education. In fact, my larger family was probably disappointed that I didn't choose to do medicine or engineering, which were more popular choices. But you have to put this in the context of the times: When I was growing up, many women would get married when they were 22 or 24 and start a family. Even if they had chosen to do a professional degree, they didn't really pursue a career. It's different now, of course. Nowadays, young women in India are much more serious about having a career.

> "I just thought a research career was the most fascinating thing in the whole world."

FOLLOWING THE DREAM

Where did you do your PhD?

As a university student, I had majored in chemistry on the advice of a colleague of my father. But what I really wanted to do was to study genetics and biology, so I next entered a master's program in biochemistry. Then I got the chance to do summer training in a place called the Centre for Cellular & Molecular Biology.

Up until that point, I had thought I was going to do my PhD in India. I had never considered anything else. But when I went there I was exposed for the first time to a series of journal clubs about *Drosophila*, and I decided that I had to work on flies. So, I took my GRE tests and was fortunate to be accepted to a good program at Brandeis University, where I worked in Kalpana White's lab.

PHOTO COURTESY OF SUCHETA KULKARNI

Sandhya Koushika

***So you fulfilled your dream of working on* Drosophila…**

Yes, and let me tell you, the flies didn't let me down. I worked on a gene called ELAV—embryonic lethal abnormal visual system. A prior student had cloned it and shown that it was a neuron-specific, RNA-binding protein. It had some very interesting mutant phenotypes, and, for my thesis, I identified some of the genes that it regulates.

Why did you switch to working on* C. elegans *as a postdoc?

For two reasons. One was that I had become interested in axonal transport, and I wasn't convinced that *Drosophila* was the best genetic model to study this problem. *C. elegans* seemed to be a good choice because it is transparent, so I could combine genetics with live imaging. That's a very useful tool if you're interested in the process of transport. The other reason was that, by the time I got to the middle of my PhD, I had become severely allergic to fruit fries!

Published April 1, 2013

Text and Interview by Caitlin Sedwick
csedwick@gmail.com

For my postdoc, I worked with Michael Nonet at Washington University. He was more interested in synaptic development and synaptic function, but he was willing to let me work on axonal transport. I learned an enormous amount from him.

BUILDING COMMUNITY

Was it difficult establishing your own lab?

I returned to India in 2005. My husband and I had both been looking for new jobs. We had been living in different cities, but we had one child already and another on the way, and we wanted to be in the same city. That was easier to do in India than elsewhere, and I also thought it would be a nice adventure to come back here.

I certainly had less money than the other places where I had had job offers. So, for instance, we washed and reused disposable Petri plates for years, because if we used all the money we had on getting new Petri plates we would have a limited budget to do other experiments.

When I started my lab, we were the first worm lab in the institute and the second worm lab, at that time, in the country. So certainly there were challenges, but I would say that, all around, it was a very positive experience. The climate in India is very different now. There's a lot more money and lots more support from institutes. The government is also now doing a tremendous amount to foster research, and that is wonderful to see.

PHOTO COURTESY OF DR. UPENDRA KULKARNI

Sandhya's daughters share her passion for reading.

Are there more worm labs in India now?

There are. Isn't that amazing? There are seven labs now, and I think an eighth person may soon be returning to India. If this person returns, they'll be the third *C. elegans* neurobiologist. It would be terrific because it would give us a local community and local colleagues where students can get feedback.

So the community is expanding, and I'm trying to do my part to help. I get letters every day from people asking for help with their research projects. It's just not feasible to collaborate with everyone, but I like working one-on-one with people. So, whenever I can, I tell them to send someone to my lab so we can train that person on basic things such as *C. elegans* husbandry and laboratory technique.

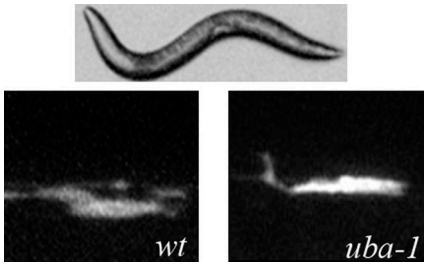
> "We're well poised to start telling stories about how axonal transport might be regulated."

You brought the problem of retrograde axonal transport back with you to India…

I did, because that was what excited me. There were some questions that I really wanted to answer and methods that I wanted to develop. Having my own lab finally gave me the chance to be able to expand in these directions.

Let me give you an example: I was initially interested in looking at retrograde axon transport, and I wanted to label endogenous proteins from the synapse. Mike Nonet and I had talked about it, but I was finally able to publish that paper and bring it to completion only in my own lab, because there was only one of me to work on things in Mike's lab and that was not the main focus of his group. We can now look specifically at what's coming from the synapse, and we are trying to develop a genetic system that will let us track endogenous proteins leaving the synapse.

Then I wanted to set up a good system for live imaging of transport in the worm. Very early on, we figured out that anesthetics were a big problem because they can dramatically alter transport dynamics.



IMAGES COURTESY OF BIKASH CHOUDHARY AND NIKHIL MISHRA

Koushika's lab has shown that Kinesin-3 accumulates in the synapses of worms deficient in ubiquitin-mediated degradation (*uba-1* worms, right) compared with wild-type (left).

But I had heard about microfluidics, and I found a very nice collaborator who was as adventurous as I was. Together we developed our own microfluidic chips to immobilize the worm for light microscopy without anesthetics. So we've been able to make *C. elegans* a useful model to study the phenomenon of transport.

We've taken advantage of local collaborations to generate new technologies that we can then use to address a given problem or mutant in as many ways as possible. Now we're well poised to start telling stories about how axonal transport might be regulated during development and how it might contribute to neuronal function. Those are the long-term questions that I'm interested in. And we're not limiting ourselves to studying only the worm; we're branching out to studying other organisms as well.

1. Koushika, S.P., et al. 1999. *Mol. Cell. Biol.* 19:3998–4007.
2. Koushika, S.P., et al. 2001. *Nat. Neurosci.* 4:997–1005.
3. Surana, S., et al. 2011. *Nat. Commun.* 2:340.
4. Mondal, S., et al. 2011. *Traffic*. 12:372–385.
5. Kumar, J., et al. 2010. *PLoS Genet.* 6:e1001200.