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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Prachee Avasthi

Prachee Avasthi studied Molecular and Integrative Physiology at the University of Illinois at Urbana-Champaign. She received her PhD in neuroscience in 2009 from the lab of Wolfgang Baehr at the University of Utah for her work on the control of membrane protein trafficking in photoreceptors. Prachee then moved to Wallace Marshall's group at the University of California, San Francisco, for her postdoc, where she studied ciliary assembly and the regulation of ciliary length. She set up her lab at the University of Kansas Medical Center in 2015, and relocated to the Geisel School of Medicine at Dartmouth in 2020, where she is an Associate Professor of Biochemistry and Cell Biology. Her group investigates the biogenesis of cilia and the coordination of actin- and microtubule-based trafficking.

What inspired you to become a scientist?

Actually, doing research as an undergrad – before that I didn't really know that a research career was an option. I worked in a whole variety of different labs, largely in neuroscience, and I fell in love with research; trying to understand how to figure out what we know and what we don't know, synthesizing our knowledge and coming up with a meaning for the project I was doing was really fun and exciting. I majored in physiology, as at the time there was no undergraduate neuroscience major, but then I looked for neuroscience PhD programs and ended up working on photoreceptors, which are neurons.

Did your interest in cilia come from studying photoreceptors?

Yes. At the time, almost all of the research in photoreceptor biology was on phototransduction, looking at how light is turned into an electrical signal. Every single gene that was involved in phototransduction was cloned and knocked out in mice, so we understood this process in a great level of detail. But around that time, the outer segment of the photoreceptor was starting to be known as a highly modified cilium. Since we had so much information about the signaling components that were trafficked through this modified cilium, it was really a ripe time to start studying the photoreceptor as a trafficking and cilium problem. But then, when trying to understand this problem, nearly all the fundamental discoveries about cilia I read had been made in algae, which is a really elegant system, and almost everything about ciliary assembly is conserved in this organism. For my postdoc, I knew I wanted to work on ciliary trafficking in a model where I could really get at the mechanisms, and I fell in love with *Chlamydomonas*.

One focus of your research is studying the role of actin in the biogenesis of the microtubule-based cilium. Could you tell us where the work is heading and about any challenges you encountered with the projects?

Actin has a large number of functions in every cell, so the challenge is not figuring out whether it is involved in a certain process but dissecting what its roles are in different cellular contexts.

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Prachee Avasthi. Photo credit: Kurt M. Wehde.

One new direction that we're now moving into is using actin-binding proteins to dissect the functions of actin in different places in the cell as it pertains to ciliary biogenesis. In one of our recent stories, we came up with a totally new model for how ciliary protein trafficking happens. We are still just starting to understand the system but think that the ciliary proteins are sort of in a reservoir in the plasma membrane, where they can be reclaimed for early ciliary biogenesis through endocytosis. We're now also doing live-cell imaging to look at both actin dynamics and myosin dynamics, and to actually understand how these things are functioning in real time. An initial challenge when studying actin was that there were no good actin visualization strategies in *Chlamydomonas*; even though it's a conserved protein that has been studied before in this species, none of the typical tools that people use to visualize actin worked. So my lab put a concerted effort into making that happen, which took five years, but this completely unlocked all of the biology.

Looking back at the time when you started your lab, what was the biggest challenge and how did you overcome it?

One of the biggest challenges was isolation – going from a group with a cohort of postdocs to suddenly being alone in my office and feeling acutely isolated. And this had nothing to do with the environment at the university, which was great. Rather, I think there's a misconception of how science needs to be done; many of us, because of that 'independent' position, have this idea that we need to be alone and do it all on our own. But while independence does give you the freedom to go in your own directions, this shouldn't be a solitary endeavor. The realization that I didn't need to solve all the problems of a new PI alone led to the inception of the NewPI Slack community – so my solution was building a

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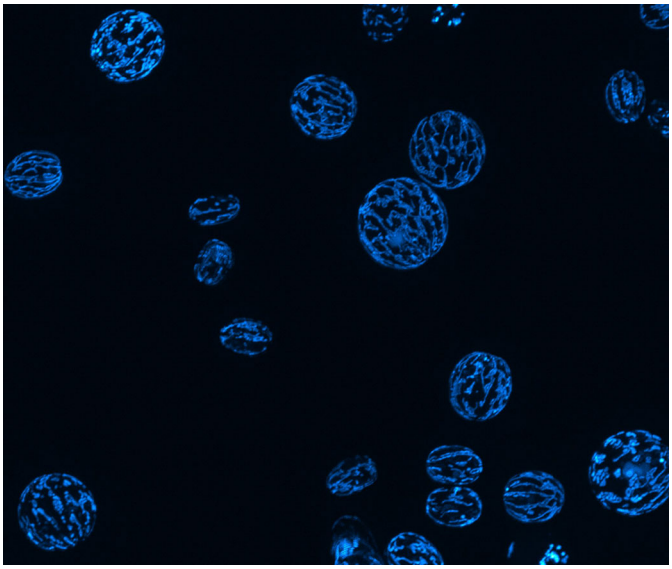

Visualization of a fluorescently tagged mitochondrial enzyme in *Chlamydomonas*. Image credit: Larissa Dougherty.

solution. I've also relied on different mentors that I have selected, for example, for getting feedback on my grants or advice about mentoring.

Regarding selecting mentors, what advice would you give researchers who are just starting up their lab?

My advice is to be proactive, find people who are good at a certain thing and ask them to be your mentors in that specific realm. There are really no limitations on who those people can be, and you shouldn't be limited by geography. This is especially important for certain communities that are highly underrepresented, either scientifically or otherwise. So when selecting mentors, I'd encourage everyone to realize that they are part of a global scientific community and that, instead of just picking one mentor for everything, it's useful to build a team of mentors around yourself. It's also crucial to choose people who value the same things that you value, otherwise the advice you will receive might not be right for you. I'd also add that when you have a really good reason to connect to someone and know exactly why you need their help, they are much more likely to respond, as the connection will be valuable for them too.

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You are a huge advocate of preprints and one of the directors of ASAPbio. Could you tell us how you became so passionate about promoting preprints and got involved with this organisation?

From watching the first ASAPbio meeting in 2016 on my sofa at home. I didn't know anything about preprints before that, but I was immediately taken by the idea. I had just started my lab about a year earlier, so I was finally responsible for deciding how we publish our research, and preprinting just made so much sense. Why would we do it any other way? Why not make our work available as soon as we're ready for people to see it, and then ask for feedback, instead of being at the mercy of some other systems? And we could still submit our work to a journal if we wanted to, so there really wasn't any harm. There were so many upsides that it seemed self-evident to me that preprinting was a good idea, and I couldn't shut up about it. At the time, I also had the opportunity to start a journal club for a course I was teaching and thought 'why not do a preprint journal club?' This turned out to be a wild success, because we sent the feedback to the authors, who really appreciated it and were thrilled that someone had carefully read their preprint. Later, I cold-contacted Jessica Polka, the Executive Director of ASAPbio, and asked her whether she would be willing to organize a session on preprints with me at the American Society for Cell Biology conference. She said yes, and from then on I've been a part of ASAPbio and one of their directors for a couple of years. The lessons here are that you don't need to know someone or be somewhere to get involved in such things, or wait for permission to do stuff if you have a good idea.

A policy of your lab is to post every manuscript as a preprint before submitting it to a journal in order to improve it following feedback from the community. What has been your experience with this approach?

Actually, the first time we posted a preprint was right before a big cell biology conference. We put the preprint link on our posters and told the people coming by that they could find a lot more data in the preprint and if they read it they should let us know what they think. We received a lot of good suggestions and ideas, many of which we incorporated when we submitted the work to a journal. And the paper actually got accepted without revisions – it might have been serendipity, but there was no way we could not continue following this approach afterwards! Of course, not every paper has been like that, but importantly, this approach completely removed the fear and anxiety from the process of getting the work published in a journal. We're never worried anymore about what kind of comments we will get from reviewers, because we've already shown it to so many experts. We also really get to enjoy the moment when we make our work public and tell the world about it, as opposed to the time of journal publication, when we might be sick of the paper and just want it to go away.

You are very active on Twitter. Where do you see the value in social media for science and scientists?

I love Twitter and think it's sort of an indispensable tool for a scientist, at very least for discovery of new science. There is a huge amount of literature out there, and I don't think that we can expect people in these busy times, with everyone overstretched, to just happen to stumble upon our work – even if it's really interesting and important for the field. In fact, when you look at when certain studies become part of people's awareness, it often takes years. This is why, when we post a preprint, we will always put out a Twitter thread about it where we not only summarize the science but also explain our thought process and why we did certain experiments, or what paths we took along the way that didn't make it into the preprint. This enriches the story so that people sort of get sucked in and understand the work better and are able to give us useful feedback. Twitter is also an amazing way to talk to experts, recruit students and in general interact with people you otherwise wouldn't necessarily have a chance to meet. We really shouldn't be limited by the old-fashioned way of making new scientific connections through physically flying to a conference and bumping into someone.

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Through Twitter, many people have also learned that you are co-founding a new institute for the study of emerging research organisms, which is planned to launch later this year. Could you tell us a bit more about the idea behind setting up Arcadia Science?

All of us who have worked with different kinds of model systems that are not humans or mice have faced many challenges. The research communities are small, so there often isn't a critical mass in the field to advance technologies that are crucial for making progress. But as a single lab, it's difficult to push forward both the tool development and the biology. Moreover, even though there is a general understanding that basic research is important and that many immense discoveries have come from studying strange organisms where evolution has solved many biological problems, it's hard to get funding to work on really fundamental processes in a weird system. So, we're launching this institute, which will be based in Berkeley, USA, to fill these gaps. We want it to be a very outward-facing institute, and we really hope to be able to unlock new technologies for people in the small research communities. For example, we'll have technologists who will be inventing new solutions for people so that they can then focus on the biology. We're hoping to be able to make a fundamental change by putting a lot of effort, energy and money into this type of really important science. We also want to make sure we push ourselves to break out of the limitations of the journal article. We will therefore be publicly releasing our data sooner, won't be publishing in journals and will solicit open feedback. Without other proxies of quality, we will have to make our work useful to others and stimulate robust public discussion around it – all things we believe are good for science.

If you could change one thing in academic research culture overnight, what would that be?

I would change the selfishness, all across the board. I think we've normalized that it's okay to be selfish for our career advancement and therefore feel that we can excuse behavior that's bad for science, bad for society and bad for other people if it helps our career. I know a lot of people who don't operate that way, but I think we should all try to do something that's better for science and the people around us right now, instead of thinking that we will change once we get into an imaginary position of power where we'll feel comfortable. And when people say that certain actions are not rewarded by 'the system' and that they will wait for the incentives to change, we have to remember that all of us are 'the system', so we should change how we do things from the bottom up. When behaviors change, incentives do follow.

"…I think we should all try to do something that's better for science and the people around us right now, instead of thinking that we will change once we get into an imaginary position of power where we'll feel comfortable."

Finally, could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

I spent a lot of my pre-school years travelling around the world with my dad, my mom and my older sister. My father was in the merchant marines in India; he was an engineer on an oil tanker, and there were times when the family could go on commercial ships with him. So before I was school age, I think I travelled around the world more than I have since then!

Prachee Avasthi was interviewed by Máté Pálfy, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.