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INTERVIEW

Transitions in development – an interview with Rashmi Priya

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Rashmi Priya is a Group Leader at The Francis Crick Institute in London, UK. Her research combines genetic, cell biological and biophysical approaches to understand the complex morphogenetic events of organogenesis, using the zebrafish heart as a model system. We met Rashmi at the Crick to learn how she got started as a researcher, and to discuss the challenges of starting a lab in the middle of a global pandemic.

Let's start at the beginning: what got you interested in science in the first place?

Growing up, science was never in my career plan – I was more interested in journalism and civic engagement. But in the India of the early 2000s, we were encouraged to consider traditional better-paid professions, like medicine or engineering. So, I ended up taking science at university, and I enjoyed it, but I didn't want to be a doctor or an engineer, so I was kind of stuck. It may sound naïve, but I didn't know that research as a career existed. There weren't any scientists in my family. I did my high school and university studies in a very beautiful remote corner of India, surrounded by mountains and jungles, which was great, but the environment was not conducive to finding out about these kinds of career options.

I came into research by chance. I remember it was a winter morning in 2004: I was reading the newspaper and there was an article in which the President of India, Dr Azad, talked extensively about the Human Genome Project. This piqued my attention, and I started reading more about it. This was the first time I realised that you could train to be a scientist, and that research existed as a possible career path. But then I didn't know how to go about getting on this path – how one applies for a PhD, or what it is like to be in a lab. Here again, my morning newspaper reading ritual came to rescue. I saw an advert from the Department of Science and Technology, offering 2-month fully paid research fellowships. It was a highly competitive program, and they only offered eight to ten positions. I applied, and magically I got selected. I was placed in the Biophysics Division at the Saha Institute of Nuclear Physics in Kolkata, and this was my entry into research – those 2 months changed my career and my life in many ways.

Early in your career, you worked on quite a wide range of topics, from malaria parasite replication to cell-to-cell adhesion. What drove your choice of research topics and labs as a graduate student?

Again, this was all a matter of finding opportunities where I could gain research experience. My time in Kolkata made me realise two things: firstly, that I enjoyed being in the lab and I wanted to do a PhD; and secondly that I needed to work on my CV, because it really wasn't competitive. So, my idea was just to get more research exposure, and I wasn't really limited by the topic. I applied to various labs and found a position in the Dhar lab at Jawaharlal Nehru University, New Delhi, that was working on replication mechanisms of the malaria parasite. Later, I was awarded a research fellowship and moved to Mumbai to the cancer research institute (CRI-TMC), where my work was focussed on cell biological aspects of cancer metastasis – and that was my entry into the field of cell-to-cell adhesion.

Moving to Australia for my PhD was a personal decision because my partner was going there. Because I'd become interested in cell adhesion, I decided to approach Alpha Yap (University of Queensland), and he invited me to give a talk and to spend a day with the lab. And by the end of the day, I knew I wanted to do my PhD with him. Alpha is simply great, and the lab environment and the infrastructure were amazing. I applied for a PhD fellowship and fortunately got funded, and things started rolling. So, yes, there was no clear path in front of me as such; all along the way I have been actively seeking better opportunities to learn and trying to make the most of them.

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What then led you to a post-doc with Didier Stainier, working on heart development in fish?

This was an informed decision! I had a productive PhD with Alpha, trying to understand how cells change their shape and remain attached to each other by focussing on the adherens junctions. And

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while I thoroughly enjoyed teasing out these mechanisms in cells, there were moments when I used to wonder how all these pathways and cellular behaviour really work in a living organism. So, by the end of my PhD, I knew that I wanted to do *in vivo* cell biology and understand morphogenesis in a complex setting, and zebrafish is an ideal system for this. I spoke to some of my zebrafish colleagues at the institute, and they were all admirers of Didier's work. So, I approached Didier, and he replied literally within minutes. We met on Skype, and we had a very engaging scientific discussion about the morphogenetic aspect of heart development. And Didier is known to be very supportive towards career progression of his trainees, and many of them have gone on to successfully launch their own labs. I knew that I would learn a lot from him and in the autumn of 2016, I moved to Bad Nauheim to start my post-doc.

What were the most important considerations when you were looking for group leader positions? How did you choose the Crick?

The things I was mainly looking for were an open dynamic environment, strong commitment towards early career group leaders and solid investment in fundamental science. The Crick met all these criteria, and the added advantage was the rich scientific ecosystem of London, which very few cities can boast of. I really enjoyed the whole interview process at the Crick and left feeling enriched and valued. So the decision was an easy one!

How has the experience of transitioning to a group leader been?

The word is 'intense'. It's been almost a year since I started the lab, and I think nothing could have prepared me for this. In the beginning, I was trying to do everything perfectly at the same time – lab establishment, management, recruitment and research, which is just not possible. So, initially the actual research took a bit of a back seat, and that left me feeling confused. I took some time to realise and accept that a significant part of my job is going to be non-scientific and management related.

Also, it can get lonely at times in the beginning, and this was amplified by COVID. As a PI, you arrive in a new country at a new institute and can end up spending hours in your new office alone, rather than being in a lab surrounded by people. Obviously, this gets better as the team grows and one starts to build a community. So now I am just looking for an excuse to escape my office!

Another thing that affected me (and still affects me) is imposter syndrome. Even though I was in a very supportive environment I felt a constant need to prove myself. I suddenly felt the need to behave like a 'superwoman' and that I couldn't express my fears and weaknesses, which was much easier to do as a PhD or post-doc. So it all got very exhausting. Anyway, early on I realized that this could not work and started bothering people – talking with my mentors, inviting my colleagues for lunch or coffee meetings – and that really helped.

What's been the best moment?

There have been many; I can't pick out one. It's the small things – arriving in the morning and seeing my team chatting and laughing, the intense discussions we have in lab meetings, when we got our first transgenic line made, when a lab member presented their work for the first time, and so on. Also, our research is quite exploratory, and recently we have had to reframe some of my initial hypotheses. It might sound strange to be excited about this, but it means something else interesting is happening and perhaps we are in for a surprise!

And what about the most challenging? You started in early 2021 in the middle of the pandemic, so that must have been pretty tough...

Yeah, I think those of us who started our labs in the last 2 years – the 'pandemic PIs' – all have quite wild stories to tell. My last job interview was at the Crick in March 2020. And literally while I was flying back from the UK to Germany, everything shut down. So I spent the whole of 2020 juggling the revisions for my post-doc paper, job offers and recruitments, all within the four walls of my apartment without much interpersonal interaction. By the beginning of 2021 I had to move my personal and professional life to the UK, which under normal circumstances is stressful, but with the background of Brexit and COVID, it was absolute chaos!

I was also navigating two different realities at the same time – embarking on my dream career while, back home in India, things were gloomy as the COVID situation was getting worse and I could not visit them. Having said that, I still had a relatively easier pandemic than others. I had a job, no caring responsibilities and I remained healthy. I also had a lot of support from the Crick and the operations team did an excellent job in getting us up and running very smoothly.

Can you summarise the research themes of your group?

Broadly, we're trying to understand how simpler structures like cell sheets build intricate anatomical structures like tubes and ridges during organogenesis. We use the developing zebrafish heart as our model system, as it's highly accessible and amenable to imaging, genetic and biophysical manipulations. More precisely, we're working on cardiac trabeculation, whereby the heart transforms from a hollow lumen into an intricate 3D topological structure filled with ridges called trabeculae. Trabecular ridges make the heart an efficient pump and are critical for its function. While there is a lot of information on the genetic pathways required to form trabeculae, the underlying cell biology has been largely missing, and this is where we come in. We use a range of interdisciplinary approaches to dissect trabecular morphogenesis, across time and space. Some of the questions we're working on are: how cells chose their fate, how cellular processes happening at the single cell level give rise to macroscopic structures, how trabecular meshwork density and organization are constrained, how organ form (geometry) and function (flow) informs this morphogenetic transition, and how inter-tissue interactions shape these structures.

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What are the most exciting areas in your field at the moment?

It's the best time to be a developmental biologist! With the introduction of modern imaging and -omics tools, mathematics and physics, the possibilities are endless. We can visualize development of a beating heart at single cell resolution *in situ* (Priya et al., 2020; Taylor et al., 2019), and can also build somitoids that recapitulate oscillations of the segmentation clock *in vitro* (Sanaki-Matsumiya et al., 2022). Morphogenesis is challenging and complex, and so for long, we have been using simpler accessible systems to understand it, but that rarely gives a full picture. So now, there's a growing realisation that we have to embrace the complexity and study morphogenesis *in toto*, which really inspires me. And some

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of the recent studies have shown us that, with these modern tools, it is indeed possible to dissect this multiscale problem in a robust quantitative manner inside living embryos (Fukui et al., 2021; Munjal et al., 2021; Naganathan et al., 2022). I'm also enthusiastic about the various *in vitro* models of morphogenesis – the various '-oids' – as their modularity and amenability is going to be extremely informative.

Your research is quite interdisciplinary – what do you see as the benefits and the challenges of bringing together different fields?

It's challenging, but the benefits outweigh the challenge so I would totally recommend it! Entering a new discipline is a steep learning curve, so one has to be open and ready to do the hard work, as, basically, you are starting from scratch. You need to learn the language of the new field and, at the same time, simplify your own language and ideas so that new field can embrace them. You need to read vigorously to identify the interesting problems. At the same time, a little bit of naivety helps, as you don't carry the baggage of the field and you are braver to do those odd experiments, which are usually the most interesting ones!

How important do you think mentorship is in navigating an academic career? How have you benefitted from your mentors and what approach do you take to mentoring your team?

It's extremely important – I'm where I am because of my mentors, and because they trusted my capabilities much more than I did. I've learned different things from each of them. Early on, my Masters supervisor, Ashraf Dar, was very strict about scientific rigour and discipline – like how to label your samples and tubes. I didn't enjoy that as a young student, but it set the tone for me, and it stood me in good stead. Then, I was very fortunate to work with Alpha during my PhD, who is extremely generous and supportive! He will be out there as your strongest advocate but when it's needed, he'll give you that extra gentle nudge to push you forward. And then I went to Didier's lab, which gave me all the freedom to build my research plan and prepared me very well for the next transition, in a safe environment. I learnt from him how important it is to balance both the bigger picture issues and the small details – write the strongest cover letter and prepare immaculate figures with all the panels aligned.

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In terms of my own mentorship style, I'm still new to this, but one thing I know is that there can't be a recipe to it because different people have different requirements. I think my job as a mentor is to make them believe in their potential and ensure that they have everything they need to accomplish their goals. I believe it's a long-term investment – not only do we need to advocate for them but also to help them prepare for those opportunities. I am still learning how to balance the yin and yang of mentorship.

What advice would you give to people starting their own labs?

It can get overwhelming at times in the beginning, so look out for yourself and ask for help when you need it. I'm not good at this – I will write an email with subject 'help', and it sits in my drafts folder for days as I don't want to bother people. But every time I have hit the send button, I've found that people are always willing and happy to talk and give advice. So recruit mentors for yourself and perhaps different kinds of mentors for different things. Also, you will get a lot of advice, but you have to be ready to trust in your own instincts, make mistakes, learn from them and move on.

I'd also give one piece of practical advice: spend time establishing what I guess I'd call the lab management infrastructure very early on – plasmid inventories, data storage systems, standard protocols and so on. It takes a lot of effort and might feel like a waste of time, but it will pay off in the long run.

Finally, is there anything Development readers would be surprised to learn about you?

I don't know if it's surprising, but I took a brief formal training in Hindustani classical music, and at one point I was pretty serious about it. I listen to classical music every day as it helps to keep me grounded. There are ragas for different times of the day, and they do affect you. I'm getting quite interested in the science behind this, but wish I had more time.

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