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INTERVIEW

An interview with Swathi Arur

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Swathi Arur is an Associate Professor for the Department of Genetics at the MD Anderson Cancer Center, USA, where she uses multidisciplinary approaches to understand female germline development and fertility. She has received numerous accolades, including the MD Anderson Distinguished Research Faculty Mentor Award in 2017. In 2020, she was elected to the American Association for the Advancement of Science (AAAS). Swathi joined the team at Development as an Academic Editor in 2020, and we met with her over Zoom to hear more about her life, her career and her love for *C. elegans*.

Let's start at the beginning – when did you first become interested in science?

I grew up and went to school in Bangalore, in the southern part of India. I think my first interest in science was triggered by my middle-school teachers, who really applied a lot of critical thinking to learning, whether it be English literature or biology or mathematics. These teachers inculcated this idea of 'what is my question?' and I found this analytical approach to education very attractive – even early on. It's solving puzzles; asking questions and trying to answer them. Although I didn't realise at the time, these were scientific approaches that excited me. I'm lucky because I found teachers that have fostered this, even as an undergraduate and in graduate school.

Did this pursuit of answers influence your decision to do a PhD? What were your research interests during that time?

I did my undergraduate in microbiology, because it was one of the subjects being offered at the time in India. Unlike biology and biochemistry, microbiology was fascinating to me because you could really see the microbes under the microscope. As a child or young adult, I found the process of being able to look at something fascinating, and I preferred this over working with molecular material that I couldn't see.

I started my PhD in microbiology in New Delhi trying to understand the pathogen *Helicobacter pylori*, which at the time was an emerging pathogen. I joined the Department of Pediatric Gastroenetrology at the All India Institute for Medical Sciences, and I joined that department because of the work done by Professor Bhan, who became my graduate advisor and who unfortunately passed away last year. He was a physician scientist who really fostered in his trainees his love of science. I think he didn't really care what I wanted to do – he wanted to know why I wanted to do it; what did I want to learn?

So I started out trying to understand this emergent pathogen: how it infected children; how it infected the gut. But what was fascinating about this bug was that it could either cause cancer or cause ulcers – you didn't get the same person with both. I then became interested in trying to understand how the microbe communicated with the host, which led to the second half of my PhD. I realised that the microbe was fascinating, but the human was more fascinating! I wanted to understand how the body reacts; how did it learn to live with the organism as a symbiont versus a difficult pathogen?

Did your drive for visualising science play a part when choosing a post-doc? Does it still influence your research today?

Yes, that is still something I follow up. I started my early post-doc – more like a postgraduate – at the University of Connecticut with David Han working on apoptosis mechanisms using an integrated approach of quantitative mass spectrometry with cell culture. We identified a new molecule that appears on the outer plasma membrane upon initiation of programmed cell death, using these technologies. And then we wondered 'are these findings relevant *in vivo*?'. Identifying new molecules doesn't really crack development, it doesn't really cure disease until one understands its relevance *in vivo*. So we sought out another junior faculty person, William Mohler, who was just starting his lab at the University of Connecticut at the time, after coming from John White's lab at the University of Wisconsin. William Mohler had started teaching worm (*C. elegans*) genetics and I fell in love with it. It was beautiful! At that point, I knew that this was what I was going to actually go on to do as a post-doc. It's interesting, because I went on to do my post-doc with Tim Schedl at Washington University in St Louis, Missouri, where the state motto is actually 'The Show-Me State'. That was quite fitting because I was very much like, 'show it to me'. That's how I ended up with *C. elegans*, imaging

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and asking questions that I could visualise. The idea of 'following what you see' has never died – I think it's very much what drives my lab today. We are very much an imaging-based lab. Of course, we do biochemistry and genomics, but those are tools to answer fundamental questions and those questions are driven by what we see.

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How was that transition, not only moving between different systems but also moving between different countries?

I came from New Delhi, a city of 11-12 million people, to New Haven, which has got about 50,000. That was an experience! I wasn't expecting a lot of things. For example, I felt like people really didn't understand what I was saying because, even though I spoke English fluently, my accent was very different. It worked out well, though, because the people that I worked with were very generous and kind, and they walked me through everything. I felt it was a very collegial and beautiful environment. I felt like I could not have navigated it without my lab mates, without my mentors. They also helped me to navigate the new technology; I was learning how to do mass spec and a whole bunch of things I hadn't touched before.

On the transition to moving into a new system, it was fun. When I moved from Connecticut to start my post-doc in Missouri, I went from doing cell culture biology to genetics and development – and I came from a background in microbiology! So that was quite a wide bridge to navigate. I took some graduate classes and that was very cool, because I learned so many things. It was also kind of fun, because nobody treated me like I should have known the theory already; I don't think anybody treated me any differently than any graduate student. I really enjoyed it and I thought that it was pretty empowering. It was a fun transition.

Can you tell us about your research during your time at the Washington University in St Louis?

I've always wanted to understand how cells communicate with each other and the environment, and how did that communication modulate their responses and their development. I was looking for a lab that was doing *C. elegans* research – I've already told you about my love for *C. elegans* – and also working with signalling and germ cells, because I think germ cells are just the most fascinating type of cell. I joined Tim's lab, because he was doing a lot of Notch signalling work at the time. I was very interested in MAPK signalling because one paper from David Greenstein's lab, who Tim had collaborated with, had shown this beautiful signalling pattern for active MAPK in the germline (Miller et al., 2001). What had fascinated me back then – and I still haven't figured out the answer to this – is that the germline is a syncytium, but the signals have very strong patterns, very much like expression stripes in fly early development. I wanted to know how you get that very strong expression pattern, and I still haven't solved that question.

You started your own group in 2010 at the MD Anderson Cancer Center, Texas, USA. How was the process of becoming a group leader?

I was already pretty independent; I'd been promoted to an instructor at Washington, which meant that I was already helping with training students in Tim's lab. The transition to a group leader is always interesting, because you go from being a very successful post-doc that almost everybody knows, to being a person with a key and an empty lab. I felt like my excitement was so high, it never occurred to me that I should be overwhelmed! Because I had met excellent colleagues and mentors in Connecticut and Washington, it was natural for me to walk up to the lab next door and say, 'Hey, this is who I am, this is what I'm doing'. I expected that they would absolutely fall in and help me out – and that's exactly what happened! I tell my trainees or other members of the department that are going through this transition, 'find an academic environment where people are very collegial and open to helping you navigate those early years'.

Those communication skills seem to have been really useful for you. Were there any other skills you felt you needed to develop?

Communication is key – I think it's everything – I'm a signalling person so, without communication, there is no body, there is no cell! I think managers need to be able to effectively understand somebody's motivation, what drives them, and that needs to synergise with your own motivations. Sometimes, conflict also leads to new ideas – that's great – I also foster disagreement, but it's getting that balance about right. I've had all of my conversations with colleagues in the pub or, if the person doesn't drink beer or alcohol, in a coffee house, because I don't feel comfortable having a conversation in my office. But with communication, I think what I had to learn was a mindset change. When I was a post-doc, I could say things and make suggestions as I was a peer. As an advisor, it took me almost a year to realise that, although I was saying similar things to people in my group, they interpreted it differently. I needed to make it much clearer that I was thinking, sharing ideas, rather than just instructing people to do things. MD Anderson has these Heart of Leadership courses, where we spent a whole day together once a month for 12 months. I took this course and I began to learn a lot more about management styles. Much like when I didn't know genetics I could set out to learn the principles, I could learn the principles here as well.

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Could you summarise the research interests for your group and how explain you became interested in those topics?

Fundamentally, what we're interested in is germ cells and how germ cells develop. I've told you about my love of *C. elegans*, but my inherent interest has always been signalling. I've told you about how, during my post-doc, I was interested in solving the expression pattern of MAPK signalling in the germline and I'm still interested in that. In attempting to solve my question, we've now gone into trying to understand all aspects of germ cell development and how signalling regulates it. We figured out that the maternal nutrition environment actually triggers activation of ERKs (Lopez et al., 2013). Really, what we were studying was the KRAS signalling pathway and an advantage of working in a development lab was that the dogma was KRAS is the most mutated oncogene – it drives cancers – yet here was a tissue where KRAS was active, not in stem cells, not in proliferating cells, but in meiosis. A cancer biologist would look at that data and think, 'oh, cancer', and a germ cell

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biologists would be like, 'oh, meiosis', but, to me, it was the same signal doing the same thing. In the worm in vulval development, it was called a fate switch, which is what Bob Horvitz and Paul Sternberg worked on. I want to understand: what is this pathway? What did it regulate? How did it do it? It was quite obvious that people were going to discover new things, because the dogma in the KRAS field, is that it's all a transcriptional fate switch. We set out to find that this can't be a fate switch, because oogenic germ cells were in a 'maintenance' phase after acquiring their fate, and most of oocyte development is transcriptionally silent. I moved to the Cancer Centre to test whether the 30 KRAS/MAPK targets that we identified (and that were conserved at the sequence level) were functionally conserved in mammalian development. We also wanted to know whether the mechanisms we had identified in KRAS-mediated regulation of germ cell development were convergent with mechanisms regulating human cancer progression. So, now, we're doing: *C. elegans* germ cell development, metabolism, cancer development and cancer progression. Who knows where else we will go in the future!

How important do you think it is for young scientists to develop interdisciplinary approaches and collaborations?

It's very important to me because it keeps me going, keeps me interested, but I don't think there's a universal rule on whether or not people should do interdisciplinary science or focus on one aspect of science. I will quote somebody much more intelligent and eloquent than me: Susumu Tonegawa, the Noble Prize winner in Physiology and Medicine in 1987 said 'it helps to try and combine knowledge from at least two different fields where people do not necessarily interact', it helps foster creativity because of convergence of new ideas and concepts. This statement captures how I feel about interdisciplinary science perfectly and I could not have said it better.

How has the COVID-19 pandemic affected your research?

At the level of actual research, I think being unplugged for an experimental scientist, it's hard, because for 4 months there are experiments that can't happen. So that definitely affects productivity, but I feel like we can still catch up. It's given us time to plan an experiment so, when we started back up about a couple months ago, I think we came back as more organised and reflective scientists. We were doing experiments that were much more thought through, because we had time to do a lot of analysis. Even though the productivity slowed down, I don't think this will be a problem in the long term.

I do think that, in terms of wellness, for my lab, trainees and colleagues around me, I think it's done a huge amount, because the social fabric suddenly wasn't there. Most of my trainees are not from Houston, Texas, so they are living here without their families and, all of a sudden, they weren't able to come into the lab, which was their major social network. What COVID has allowed me to do – with much more focus – is make sure they're all mentally doing better and continuing to be resilient. There were times when we used to only talk science, or predominantly science, followed by a little bit of social conversation. Now a lot more of our conversations start with 'how are you doing?' I'm hoping that when we go back to normal, we can continue to have a balance between the two.

You recently joined Development as an editor. Why did you decide to get involved?

First, I was very surprised! I absolutely love Development as a journal; I've published in Development; I read Development. I'm a member of the GSA (Genetics Society of America) and I truly support any kind of scientific publishing society that is trying to publish excellent science by researchers. Joining Development was cool, because I really admire and respect the other editors as well. It sounds selfish, but I thought I could learn from them about how to help publish good science, because that was an area where I didn't have much experience. I've reviewed for many journals and funding agencies, but I've never been involved with being on the other side, where you get to choose and decide on how to navigate and sculpt science. I felt that, in the process of learning, I could also pay it forward and contribute to that publishing process, because it has to come from us to fuel the science.

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What do you consider to be your role as an editor?

Well, I don't control who submits to me in the future, but I'm hoping that I can continue to communicate to people, who might not normally think of Development as a journal to send their research to, that it's a good option. I fundamentally believe that every single one of us, when we submit our work, would love to make it better; would love to make sure that it's the best version of the work we can publish. As an editor, if I have identified the right reviewers, distilled their comments and helped the authors make their studies better, I'd feel like I've done a decent job.

What types of articles would you encourage people to submit?

Anything unexpected that came from beautiful scientific method; just following the science, following the data. Some of them are usually descriptive, because it's something that's just been figured out; some of them are mechanistic because the description existed and the mechanism was unexpected. I get really excited by those types of articles, personally.

Looking forward, how do you imagine the field developing?

I think that the field will go into two different directions. First, I think we see the revisiting of old principles. I think, before, we were limited by what we could see, what we could test and what we could do experimentally. We didn't have the whole view, but now we can look again, see new things, test old ideas and continue learning. I think that, in the next 10 years or so, we will see what seem like old principles re-emerging.

The other thing I think we'll see is that, because of new technologies such as CRISPR, single-cell analysis and high-resolution imaging, there are fewer and fewer restrictions. For example, we can now take organoids and actually grow organ-like tissues on a chip, we can edit new organisms like anoeles (lizards) – animals that had never been studied in depth genetically. I expect that this will drive the emergence of a whole new set of principles.

Finally, what would Development readers be surprised to learn about you?

A lot of people might be surprised to learn about my love for Pink Floyd and single-malt Scotch. I like classical music, including Indian classical music, but I've loved Pink Floyd forever. As a postgraduate in Connecticut, there was a Pink Floyd show (that I couldn't afford), so I borrowed money to go to it. It was their last show as a band and that was 20 years ago. I just love everything about them.

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