

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Arun Shukla

Arun Shukla received his master's degree in Biotechnology from the Jawaharlal Nehru University in New Delhi, and joined the lab of Nobel laureate Hartmut Michel at the Max Planck Institute of Biophysics in Frankfurt, Germany, for his PhD. He then moved to the United States for his postdoctoral work with Robert Lefkowitz at Duke University (Durham, NC) in a very close collaboration with Brian Kobilka (Stanford University, CA). Arun became an Assistant Professor in the Department of Medicine at Duke University in 2011, before returning to India in April 2014 as an Assistant Professor at the Indian Institute of Technology (IIT) in Kanpur as a Wellcome Trust DBT India Alliance Intermediate Fellow. His research is centred on G-protein-coupled receptors (GPCRs), and he applies molecular, cellular and structural biology methods to understand the signalling and activation pathways of GPCRs.

What inspired you to become a scientist?

I have been interested in science from the very beginning. My family is oriented towards academia – my brother is a professor in physics and he had a lot of influence on my thinking during my childhood. During my undergraduate years, there was a huge buzz around biotechnology in India, so I started a biotechnology master's degree at Jawaharlal Nehru University. I witnessed people doing research in the department during the summer break that I worked in the lab. A year later, we had independent research projects where I worked on four-stranded DNA...during that time I felt I found my calling. What sparked my interest for structural biology and G-protein-coupled receptors (GPCRs) was my encounter with Hartmut Michel. He gave an invited seminar in Bangalore and, afterwards, I was telling him about my project. During that conversation he offered me a PhD position. The GPCRs are the largest class of cell surface receptors and the most important drug targets in humans, so I really liked the idea of working on this. I went to Frankfurt and joined his lab, and started studying GPCRs, which I continued to work on during my postdoctoral years and still am today.

What questions is your lab trying to answer just now?

We focus on three aspects of GPCR biology: First, how these receptors work at the level of atomic detail, by using X-ray crystallography and electron microscopy, and by looking at 3D structures. Second, we're looking for new signalling pathways and new interactors for these receptors. We have reason to believe that these additional pathways exist. Third, we're using 'designer proteins' – antibody fragments or nanobodies – as a tool for looking at the structure and the signalling of these receptors. Here, we're also trying to get these molecules in cells to rewire the signalling pathway and see whether there might be a therapeutic effect, for example by working as a ligand for a GPCR. These are our



main areas, the overall goal being to understand how GPCRs work, to look at new aspects of the receptors and to design tools in order to modulate GPCR signalling.

Are you still doing experiments yourself?

I try to do a little bit every day, but I have to guide the students and there's also the pretty significant teaching component. I absolutely love working at the bench; I try to stay close to things and also work on new ideas we're developing. For example I can take the lead on a risky project and, once the project gets going, I can hand the work to a student or postdoc so they're taking less of a risk.

After your time in Germany and the US, you set up your lab at the Indian Institute of Technology (IIT). How was the experience in attracting people to your lab?

I've been very lucky. The IITs are the top institutions in the country and are known for their really high standard and exposure, so the students joining the programme are top of the line. My graduate students have been fantastic – so motivated, so smart and hardworking. As for the postdoctoral fellows, there have been a few very bright people who have joined my lab here and I continue to get a number of good applications from people abroad who are interested in working with us. Indian science is struggling with people leaving for the US or Europe after their studies or PhD. But I think this is changing. Many funding bodies like the Wellcome

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Trust/DBT India Alliance or the Department of Science and Technology are now providing very nice postdoctoral fellowships. There's a long way to go, but things in India are changing in the right direction.

I presume it's at places like the IIT where this change has to be initiated?

Absolutely. It's still in the back of the mind of students that you must go abroad, get major publications and then you'll get a job back in India. I think that mind-set has to change. The research is moving at a different pace now in India – not at the same level as in Western countries, of course, but I think seeing people having their entire research career here in India and doing excellent research might lead to this change.

“There's a long way to go, but things in India are changing in the right direction.”

What are the challenges that you're currently facing?

One frustrating aspect is the delay in getting reagents or high-end instruments. Of course, the same instruments I would have used at the Max-Planck Institute or Duke University are available to us, but the issue is quantum of funding. The magnitude of the price of some instruments cannot be covered by the amount of funding attributed



Winning picture of a painting competition on the theme of the Empowerment of Women contributed by the students from the Shukla Lab.

here. As mentioned, the Wellcome Trust/DBT India alliance is the most generous funder in the country, but still, an entire five-year grant equals to about one year of an NIH RO1 grant. There's a significant difference, and Indian science must do better here, because at the end of the day, we're asking the same questions as my European or US peers, but the amount of funding is very different. This makes competing at the same level very challenging, but it is one thing that is hopefully changing in the future. As for the reagents, the delay in getting them makes it difficult sometimes. Again, of course we can get any reagents, but often there's a delay of 6–8 weeks until it reaches our lab. This is a situation that needs to improve.

What is the best science-related advice you ever received?

After my PhD I had moved to North Carolina to work with Robert Lefkowitz at Duke University and we started a collaboration with his former trainee Brian Kobilka in Stanford. At the time I worked there, they were, of course, both already highly regarded in the field, and in 2012 they got the Nobel Prize. But it didn't change things; even after the prize the priority was still answering research questions. Prizes come and go, but Bob and Brian didn't lose focus of what was going on in their labs. In fact, the day after the Nobel Prize was announced, we had a conference call about our collaborative research paper. As you can imagine there were camera crews in both labs, so I'd assumed the conference call would be cancelled. But both Bob and Brian wanted to go ahead with the call – in the end, both camera teams ended up filming them talking about the details of a research article! These people are absolutely passionate about their work, and focused. And this is great advice, which I try to pass on to my students. Bob offers three key pieces of advice to be successful in research: the first is to focus, the second to focus, and the third is to focus! Also, lots of people, for example here in India, count the number of publications, but it's the quality that matters. This is what we try to do to shape the direction of the whole field; to do research that defines a new direction, not just something to run the shop. I'm glad the people I work with get inspired by these same ideals.

How do you achieve a work/life balance when you're trying to establish yourself as an independent investigator?

I have been lucky to have a very supportive wife who is a trained biotechnologist. When I was at Duke University, she was working with me in the lab. Here, she comes to the lab and helps out when she's free, or she spends time with our son, who is four years old – she balances it. I'm always thinking about research, and I don't see it as a burden, because I'm so passionate about it and I just like it. However, every now and then I take a couple of days off and we just go somewhere, and I try to spend more time with my son on Sundays.

Has your son shown any interest in science yet?

Sometimes he also comes to the lab and one word that he says is GPCR, so I am really happy to hear that [*laughs*].

“...three key pieces of advice [...]: the first is to focus, the second to focus and the third is to focus!”

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

One thing I was passionate about during school and college years was journalism. I used to write a lot of articles in newspapers and science magazines. You know, I still am interested in this, as well as science

administration or, in general, a leadership role, because I believe this is an area where you can change things for the whole of science. This is still on my mind; we'll see how it shapes in the future.

It almost sounds like you're looking at a career in politics?

[*laughs*] Now that you mention it...well, I did participate in the student union elections at college, and I had some interest then. But

after that I really focused on research, and right now I don't have any particular affiliations. It was there in the back of my mind in my college days, though.

Arun Shukla was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.

