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CELL SCIENTISTS TO WATCH

Interview with Surendra Ghaskadbi – President of the Indian Society of Cell Biology

Surendra Ghaskadbi is a cell and developmental biologist who held the positions of Senior and Emeritus Scientist at the MACS–Agharkar Research Institute in Pune, India. His lab has been particularly interested in cell signalling and pattern formation during early development, focusing on using *Hydra* as a research organism. More recently, Surendra has played a role in teaching and outreach in India, and he is also the current President of the Indian Society of Cell Biology. We chatted to him to find out more about his career, his advice for junior researchers and his role as society President.

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

There was no one pursuing science per se in my family – my father was a professor of English, my mother a Marathi graduate and both of my sisters became doctors – but somehow I was always interested in animals and wanted to learn more about them. I had no inkling that I was going to become interested in science, or even that it could become such an enjoyable and useful activity.

How did you then become interested in cell and developmental biology?

I was lucky to go to one of the better colleges in the area that had a very strong science focus. Ahmednagar college had good departments in zoology, botany and biochemistry. Initially, I opted for microbiology, along with zoology and chemistry, because microbiology was very popular at that time – it was fashionable. But I soon realised that I liked studying animals more than microbes, so I chose to focus on zoology. I then studied entomology for my MSc. The other influential thing that I realise in retrospect is that we had a very distinguished biochemistry professor at my college – Professor John Barnabas. He was interested in the evolution of haemoglobin, and to study this, he used more than 50 species of vertebrates belonging to different classes. He and his group built phylogenetic trees based on amino acid sequence changes in haemoglobin molecules. His research, and particularly the animals he used, excited me and inspired me to pursue a career in science. After that, I moved to Pune University to do my MPhil, where I worked on the chromosomes of shrews and squirrels.

Soon after this, while I was doing a teaching job in a local college, I came across Professor Leela Mulherkar. She was an embryologist who had returned to India in the late 1950s after studying in the Institute of Genetics in Edinburgh with Conrad Waddington. She had worked on the chick embryo, doing lots of transplantation experiments, and she started teaching experimental embryology for the first time in India, using locally available materials. I had the chance to work with her for my PhD, and that's when I became interested in embryology. We looked at lots of different model systems, like chick, frog and snail embryos, as well as *Hydra* and sponges – whatever was available really.

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Surendra Ghaskadbi

What did you study during your PhD and postdoc?

I was looking at the cellular and teratological effects of a mould secondary metabolite called cytochalasin H, which was somewhat similar to cytochalasin B but had different effects on cells. Professor Mulherkar had initially become interested in teratology after the thalidomide tragedy had emerged as a big problem in Europe. She studied the teratological effects of several chemicals. Working with her was interesting and illuminating. In addition, I learned a lot of laboratory techniques. After a short postdoc with Professor Sohan Modak, I became more interested in the basics of development. Of course, interfering with normal development by various means, at organismal, biochemical, cellular and molecular levels, remains to be one of the most popular and rewarding approaches to study normal development. In fact, we know a lot about normal biological phenomena by studying the abnormal.

One of the things that I would like to mention is that, for multiple reasons, I have never done a formal postdoc abroad. On the one hand, this meant that I was not able to learn many of the modern techniques that were being used at that time. But it did mean that I could get a faculty position quite early on in my career. I was also very comfortable with tackling problems locally, both in the laboratory and at the administrative level, because I was used to the environment in India. Many people who did postdocs abroad and got used to the facilities, support and granting systems in other countries found it difficult to find their feet when they returned to India. Obviously, things are quite different now, but in the 1980s it wasn't easy to do science in India, so I think staying here proved to be an advantage for me.

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How did you decide what direction you wanted to go in when making the transition to setting up your own research group?

While working with Professor Mulherkar, I got interested in development, especially the phenomenon of neural induction. I was trying to understand the kinds of proteins and genes that participate in neural induction in chick and frog embryos, and I decided that I wanted to continue looking at patterning and morphogenesis during early development. We contributed to the area over the first few years, but the problem with the frog embryo was that you could only work with it seasonally in India. So, if a reviewer asked you to do an experiment, you had to wait until the next monsoon to get embryos. Chick embryo studies were a little easier, but there was a period after the avian flu that happened in India when the quality of eggs – at least during early development – deteriorated. I have still not been able to understand why and how this happened as the poultry industry, overall, has been doing consistently well since after the outbreaks were contained. In addition, we couldn't do much in the way of genetics with these models. So that's when I started thinking about *Hydra*, which I had used as a part of my doctoral studies. *Hydra* has an organised nervous system, so I thought it might be a good idea to look at how one of the first nervous systems arose. But I soon realised that that was a very ambitious question! However, I did find *Hydra* to be a very attractive model: it's easy to handle in the lab, it has an amazing regenerative ability, it seems to defy ageing and it also has stem cells. There were many features that any developmental biologist would like, so I switched to working with *Hydra*. One practical consideration was that, since hardly any labs in India worked with vertebrate embryos and no labs were working with *Hydra*, I had relatively less competition within the country. Most laboratories in India at that time worked with *Drosophila*. Even now, many labs continue to use *Drosophila* as a model, although other research organisms such as the worm and zebrafish are also used widely.

In the year 2000, working with *Hydra* in India was not terribly easy as, since the late 1970s, no lab had used *Hydra* for either teaching or research purposes. We started slowly, and in the first 10 years we were only able to publish a few papers. These studies, however, provided a solid foundation for what we did over the next 10 years. While reintroducing *Hydra* as a research and teaching organism in India, I continued my work with frog and chick embryos so that the graduate students and the lab could continue 'performing' in ways acceptable to peers and administrators of science. This allowed the students and me to move on in our careers. We avoided putting all our eggs in one basket – pun intended.

My parent institute not only allowed but encouraged me to start a developmental biology group, so we were able to hire people working with other research organisms like zebrafish and *Drosophila*. I felt that putting too much emphasis on just one or two models was detrimental to teaching and research, so it was good to have this diversity. Ultimately, a model system is just that – it's one model. But organisms are all so different from each other, so if one wants to learn and teach biology, one needs to study a variety of systems. I worry that sometimes people forget this and design their research questions based on their model system when in fact they should think about the larger question first and should not be averse to using more than one model system if needed. I often see colleagues trying hard to 'sell' their model organism, which may be justified while defending a grant proposal but is unfair to students; they need to learn about organisms belonging to as many taxa as possible.

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What was the main question that your research tried to address?

We were really interested in cell–cell signalling molecules in *Hydra* since these can not only provide information about regeneration and pattern formation in *Hydra* but can also provide insights into the evolution of developmental mechanisms. To begin with, we started looking at Noggin, which is a known bone morphogenetic protein (BMP) inhibitor that's important for neural induction in vertebrates. At that time, there was no report of Noggin from *Hydra*. We identified the *Hydra* Noggin and found it to be structurally conserved, and when we ectopically expressed it in *Xenopus* embryos, we got a phenotype, which we were very excited about. But we have still not been able to pinpoint the precise function of Noggin in *Hydra*, though we now believe that it plays a role in the patterning of tentacles. We also discovered *Hydra* Gremlin – another BMP inhibitor – and have been looking at molecules like FGF and VEGF. Finding FGF in *Hydra* was not surprising, but finding VEGF was a big surprise because *Hydra* is diploblastic and doesn't have mesoderm (or blood), which is the tissue that VEGF is usually associated with. But it's very much there, and we believe that it has some role in the patterning of tentacles. We also discovered many receptor tyrosine kinases in *Hydra*.

In collaboration with my wife Saroj, who worked at Savitribai Phule Pune University, we also looked at DNA repair molecules in *Hydra*; this was the other major project in the lab. We found that nucleotide excision repair genes are all present in *Hydra*. Moreover, when we expressed *Hydra* homologues of xeroderma pigmentosum genes in human cells deficient for these genes, they could rescue the phenotype to an extent. This is particularly interesting given that *Hydra* has tremendous regenerative capacity and lacks organismal senescence. Our work so far has thrown out more questions that it has answered; however, this makes me happy rather than unhappy.

And what, in your opinion, are the most exciting questions in the field?

I think the topics of regeneration and ageing – and their interrelationship – are both exciting and important. We now know that as more complex organisms evolved, their regenerative capacity decreased, and there are many theories behind this. I don't think we have the real answer to why this happens, but understanding this could be useful, for example in the context of *in vitro* tissue and organ regeneration. Most of the molecules that *Hydra* and other organisms use for regeneration are very much present in humans, but there's still lots of work to be done to understand why humans have limited regenerative abilities.

The other area I find very intriguing is biodiversity and personalised medicine. On the one hand, we have lots of conservation, with almost all developmental and signalling pathways acting in concert. But on the other hand, we know we have so much biodiversity. How can the same set of genes make such different structures with almost unlimited outcomes? This question is being actively addressed, but we are far from finding an answer. And, in the case of humans, how does variation dictate how we might respond so differently to different medicines? Also, how do factors like the microbiome, which continuously changes in

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quality and quantity, influence physiology? It would be wonderful to find out what the connections are!

You've had your own group for some time now, so what would be your advice to someone who is aspiring to set up their own group and become a PI?

I don't have much experience outside of India, so my advice is restricted to what I've learned here. One of the things that I have seen is that, very often, postdocs start their labs and try to continue the work that they have done with their mentor, but it takes a very long time for them to become established and gain independent recognition in the field. My feeling is that if people try to do something that's unique and original to them, the work will be that much more rewarding. I know that's more risky, but one can have a couple of parallel projects – one that is less risky, so that you'll be able to publish well and your graduate students can move on in their careers, but then a second project that is a bit more ambitious and high risk, which will allow you to tackle something more interesting and satisfying in the long run.

The other piece of advice or suggestion I have relates to effective communication. Although people doing science come from all around the world, the common medium for communication is still English, so I think that young PIs really need to put effort into improving their oral as well as written communication in English. Because whatever good work you do, there is no point in doing it unless it's well presented and shared effectively with others. I often see good, established scientists with exciting data struggling to communicate their findings. They need to adjust their communication style to their audiences. I think there's still lots of work to be done here.

I gather that you're winding down your lab and doing lots more teaching and outreach – can you tell us more about this?

Yes, I had a very active lab up until 2021, but I'm no longer accepting any graduate students. I'm still associated with Agharkar Research Institute, but I spend most of my time teaching, doing outreach and mentoring all over the country. I'm also involved in writing books for schoolchildren with the intention of getting them interested in science from a young age. We need to make sure that everyone, even if they don't go on to study biology or even natural sciences, has some basic understanding of science. During the pandemic, one came across many so-called 'educated' people wearing their face masks on their chins. If only they knew and remembered the basics of infection and the advantages of using a face mask properly, things could have been a lot better.

Teaching is also one of my passions. I love to talk about biology and interact with people of all ages. I go all around the country, wherever I'm invited, to teach cell and developmental biology. I usually teach at the master's level and quite often at places where there are no developmental biology teachers. Students all over the country are equally curious and smart, and they come out with the most interesting and difficult questions. I also do some teaching and outreach with schools and colleges. I enjoy taking *Hydra* with me. When we look at them using microscopes, the schoolchildren can see them moving around and feeding – they get very excited! And the great thing is that I can just cut the *Hydra* using a sharp blade and the children can watch them regenerate over the next few days; they can easily see a biological phenomenon unfolding in front of their eyes. In fact, we ended up designing a *Hydra* kit that we provide to colleges and universities so that they can establish cultures of their own and use them for carrying out simple but interesting experiments.

You are also President of the Indian Society of Cell Biology – how, when and why did you first become involved with the society?

Soon after starting my PhD, back in 1980, I went to an Indian Society of Cell Biology (ISCB) conference in Delhi. I really enjoyed the conference and found it to be very useful: there were lots of good talks, the general atmosphere was very good and there was a lot of time allotted to posters. After that, I started going to the ISCB meetings almost every year. I always stay for the whole duration of the meeting; I'm not a great fan of the fly-in fly-out culture. I became a lifetime member of the society in 1988 and developed an interest in society matters. With time, I slowly became associated with the running of the society and started to contribute to it. For example, I organised the annual meeting back in 2008. Not everybody likes this kind of society work, but I really enjoy it. So, for me, becoming the President was no big deal – it was just part of the job.

What are the main aims and mission of the society?

Firstly, we hold an annual conference where we all meet and discuss science. We make it a point to invite some international speakers, which gives the meeting a different flavour. It's a great opportunity for students and postdocs to present their work. We made a rule to ensure that we don't repeat invited speakers for three years, and that's been fantastic, as it's allowed us to get lots of young PIs speaking at the meetings. We also have some hands-on workshops that are organised by the society, for example on embryology or microscopy. These help teachers design laboratory exercises in their colleges. The workshops take place across the country so that we can try to provide access for people across India. The society is also very interested in improving and supporting the teaching of cell biology, so we have generated some protocols for quality teaching.

And what are the main challenges that the society faces?

One of the problems is that there are very few people working for the society. Lots of people use it as a platform, for example to meet people and present their work, but getting people on board to run the affairs of the society is always a challenge. For a scientific society to function, you also need funds, but to get those funds, you need dedicated people who work continuously behind the scenes to find those funds and apply for them. It's a largely thankless job that does not translate into recognitions and awards, but it can be very rewarding and satisfying if it goes well.

If you could change one thing in academia, what would it be?

I really feel quite strongly that the charges associated with publishing are getting out of control. It is becoming a big business without checks and balances. Many labs in India find it very difficult to raise that kind of money to publish their papers. I also find it perplexing that some of these publishers get so much work out of all of us – by asking us to review papers for them for free – and they never put anything back. JCS (and the other journals published by The Company of Biologists) is obviously an exception, and I know there are also some very good society-run journals that support their communities. But most of the other journals don't do this, and this really creates a problem. There are some institutions in India that can afford to pay to publish in these expensive journals, but there are people doing equally good work who end up publishing in journals that are not really read by many people, just because they do not have any other option. It creates a huge divide.

One of the other areas I would like to see a change in is the postdoc culture in India. It really hasn't developed, despite some attempts by individuals and funding agencies. People tend to leave

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the country for postdoc jobs or move on to do something else. There are also very few clinicians doing basic biology research in India, probably because they must spend most of their time dealing with patient care, but this means that there are limited opportunities to foster collaborations between basic scientists and clinicians. I think this is also something that needs to be addressed.

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Finally, is there anything our readers would be surprised to find out about you?

I like to whistle Bollywood songs. It's a habit of mine that has become a hobby. During the pandemic, I started a small YouTube channel of myself whistling. I got a lot of support from students and friends, out of sympathy I suspect, but I now have quite a few followers. I even whistle at cell biology conferences and, so far, it has been tolerated well.

The other thing I would like to mention is that I'm a kidney donor. I donated a kidney to my wife 10 years ago, and both of us are in good health. So, we help to counsel people who are potential donors and recipients; we tell them – very frankly – what we have gone through emotionally, financially and physically, to help them feel more comfortable with the whole process. We also participate in discussions on live organ donation. The number of men who go for live organ donation is extremely small, for multiple reasons and especially in India, so we try to pass on the message that it's possible and that it's good.

Surendra Ghaskadbi was interviewed by Seema Grewal, Executive Editor for Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.