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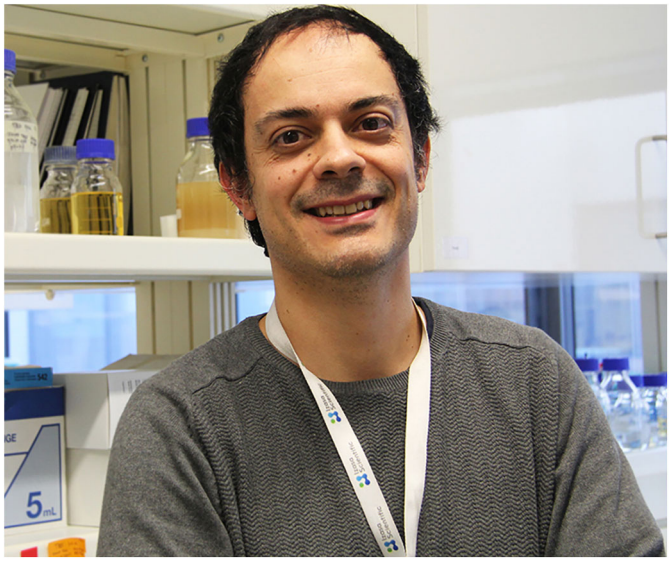
CELL SCIENTISTS TO WATCH

Cell Scientist to Watch – Eurico Morais-de-Sá

Eurico Morais-de-Sá graduated in biochemistry from the University of Porto, Portugal. After a research internship in protein crystallography at the Institute for Molecular and Cell Biology (IBMC) in Porto, Eurico moved to Cambridge, UK, to do his PhD with Daniel St Johnston at the Gurdon Institute. During this time, he studied cell polarity in the context of epithelial tissue and body-axis specification. In 2011, he was awarded EMBO and Marie Curie fellowships to return to Porto for his postdoctoral work with Claudio Sunkel at IBMC, where he used his cell polarity expertise to understand the regulatory processes of epithelial cell division. In 2018, Eurico established his own research group at Instituto de Inovação e Investigação em Saúde (i3S) focusing on the mechanisms by which epithelial cells modulate spatial asymmetry during cell division to maintain the function and integrity of proliferative tissues.



Eurico Morais-de-Sá

What inspired you to become a scientist?

I was curious about nature since I was a kid, but I only found out that I really wanted to be a scientist quite late in life. Neither of my parents has connections to academia or research, and when I was a child they were surprised that I was always playing with ants. I have good memories about doing experiments with them. When I think back about it, I didn't even notice I was doing experiments and that I already had that attraction for science. In school, I was always driven to science-related subjects. Then I enrolled in a biochemistry degree, but it was only after doing a research internship that I realised how fulfilling it was to look for new questions and answers, and that it was something I wanted to pursue. During my university years, molecular biology was having a surge. This was about the same time that the *Drosophila* genome was sequenced [in 2000]. We were starting to be able to 'edit' organisms, and I was really interested in that possibility. Of course, for my parents, I should have gone into medicine. In Portugal, they really like to have a doctor in the family. But I really hate blood and I think I wouldn't be able to deal with disease. [laughs]

With a background in biochemistry, how did you end up doing research in cell biology?

I think that I was lucky to have had an opportunity that now is very difficult to get. I enrolled in the GABBA PhD programme (Graduate Program in Areas of Basic and Applied Biology) at the University of Porto. The mindset of this programme and its mentors was that you should give freedom to your students to find out what they are happy doing in science. There were no strings attached and the students could find their real interest and pursue that during their PhD. It was life-changing for me. Prior to my PhD, I had done a research internship working in crystallography and structural biology. But I was also really interested in genetic manipulation. So I wasn't sure what I wanted to do for my PhD. In the first year of the PhD programme, we had several modules on different aspects of biology, in institutes across the country. We also had two modules in Spain; one of them was in developmental biology in Seville, in Centro Andaluz de Biología del Desarrollo. During that two-week course, I really started learning what developmental biology was. José Gómez-Skarmeta showed me developing frog eggs and I had my first contact with the power of *Drosophila* as a model organism. Also, Acaimo González-Reyes presented these big *Drosophila* oocytes with RNA polarised inside them, and I thought 'Okay, I know exactly what I want to do – I want to work on cell polarity'. It was kind of a spark, a moment of inspiration. I was lucky that I found something that was perfectly suited to my interests and the type of research I was looking into.

What questions are your lab trying to answer just now?

After my PhD work on cell polarity, I became interested in a second fundamental cell biology process, which is cell division. Now, my lab largely addresses the coordination between these processes. All cell biologists are amazed by movies of cell division. I had worked on cell polarity, which is also very visual, but I was always amazed by the assembly of mitotic spindles. One thing that stuck with me was that it must be a huge challenge for a polarised cell to cope with all major changes in the cytoskeleton happening during division. Epithelial cells have this clear functional and polarised organisation, but at the same time, they must be cohesive within a tissue and avoid any leaks. Now, we are dealing mostly with two questions. One is how epithelial cells recover their polarised organisation after cell division. Once, I gave a talk with a metaphor along the lines of how cells deal with the 'Monday morning syndrome'. During cell division, they totally change organisation, and then they must become fully functional after dividing – they must regain their polarised architecture. So I guess it is the same feeling when you do very different activities during the weekend, and then you have to get back to your job on Monday morning. Our second question is how these epithelial cells separate during division while maintaining the cohesion; how they break free (and accurately

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Eurico and his son Miguel in front of a big rainbow in Azores (São Miguel Island).

separate the genetic material) without breaking apart. Basically, we want to understand how proliferative tissues maintain their integrity and organ function. As I am a biochemist at heart, I tend to be somewhat focused on the dynamic coordination of the biochemical pathways involved. But we are also now diving a bit more into the contribution of mechanical factors.

What do you think have been some of the most influential publications in this field?

I cannot single out one publication. I think the field is evolving. Researchers have recently looked in very different organisms, both invertebrates and vertebrates, and they realised that there is a particular biochemical and mechanical coordination between dividing and neighbouring cells that is critical to modulation of tissue organisation. We now need to figure out what are the common features and what are the particularities between different organisms. I think the field of polarity, or even morphogenesis, if you consider the two broad fields we are interested in, has evolved a lot in the past decade through interactions between cell biologists and physicists, uncovering a lot of interesting new concepts. For instance, we are not immune to the trend of liquid–liquid phase transitions. We learned very recently that this plays a role in tight junction regulation, and that the core regulators of polarity, such as PAR3, can also form condensates; this adds another regulatory step in the organisation of asymmetric cell division. Even if you look into simple physical parameters, such as cell size, we now know from recent work in *Caenorhabditis elegans* embryogenesis that it can have a critical impact on PAR protein polarisation. Of course, if you think about very influential publications and work in the last years in the field, these also come through the advances in technology; not just in microscopy, but in genome editing as well. So, it's difficult for me to single out a particular paper.

Of the cell biology methods you use in your lab, which one would you say is the trickiest?

We are a *Drosophila* lab, but most of our research is at the subcellular level. We need to understand what proteins are involved and how they dynamically change localisation. As such, we depend a lot on high-resolution microscopy. In addition, we have one particular challenge; we are interested in a specific interval of time, which is when cell division occurs, and we study polarity proteins, which have broad implications in tissue organisation overall. We need to create or implement methods that allow us to manipulate function with high temporal control. We are trying this through optogenetic methods. There are several reasons why optogenetics are tricky, but I can give you a very practical one. The systems we use are extremely light sensitive, so you must ensure that there is no light of the activating wavelength in your sample until you really want to pull the trigger. It definitely requires more practice when you need to dissect small tissues under a filtered light source. Furthermore, some tools make it difficult to ensure that you create an immediate effect. For example, if you are using methods that rely on protein clustering, aggregation by itself might not inactivate your protein of interest. So, you always need to ensure that the optogenetic-based approach is giving you what you are hoping for by designing a good validation strategy.

What was the biggest experimental roadblock that you faced in your career? And how did you deal with it?

Maybe I could stay on the same subject. [laughs] I think the roadblock is the temporal control of our experiments. In fact, one of the research lines of the lab is built around the idea that we will be able to test how polarisation happens *de novo* after cell division. And for this, it is really important to test causality of the different polarity factors during that exact period. We are mostly looking at an adult organ [the ovary] and we are addressing a limited timeframe. The roadblock is that we need to have high-temporal resolution of inactivation. Optogenetics is a possible solution, but a funny story is that after trying to use optogenetics to target the polarity protein Lgl, we ended up using a temperature-sensitive allele that was isolated in a screen in 1984, and was sufficient for what we needed. So never forget the classics. Sometimes the biggest roadblock can be overcome just by going to the library. [laughs]

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What challenges did you face when starting your own lab that you didn't expect?

My career path has been somewhat different than what we would call the standard one. After my PhD in Cambridge [with Daniel St Johnston], I came back to Portugal for my postdoc with Claudio [Sunkel]. I was fortunate that he was very supportive of me applying for my own projects while I was still in his lab. Officially, my lab is a baby – we are still yet to celebrate our third birthday, but the transition was quite smooth, as I didn't have to move to a new empty space on my own. I already had some students with me and a team to start with. I think the biggest challenge was when the lab started growing. I felt I had to maximise the potential of all team members to create a fun environment. When you start with a few people, you adapt easily to their personalities. But then, as you have a more diverse group of people, the challenge is to try to adjust to people who are intrinsically very different from each other and even myself. Also, the funding landscape in Portugal is really difficult to manage. The calls for grant applications are irregular with variable funding rates. And this is a challenge for a lab that is just starting. You have to be strategic.

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How are the challenges that you're facing now different?
I'm dealing with the turnover of people for the first time. This is a turning point. My first PhD student finished last year and now I have a second student finishing. There are multiple components to this challenge. One is that you must create the conditions to support the advance in their career, of course. And you must ensure that all the knowledge and the skills that they develop are passed on to other members of the lab. There is a need for the continuity of the skills within the lab to maintain the know-how. You have to establish the lab, and then you have to maintain it and evolve. I guess that after you have been a PI for 30 years, you have seen many people coming and going and things get easier for you, but for me the turnover is a challenge that I am experiencing for the first time.

Are you still doing experiments yourself?
I like doing experiments a lot but I do very few, unfortunately. When I feel that people from my lab are about to get a very exciting result, I tend to ask them about it a lot. I want to go to the microscope with them. I always felt that you have this kick or rush of adrenaline when you get something really exciting. I think it's even bigger if you see it with your own eyes, instead of someone coming and telling me 'I have these data, but I still have to quantify them'. I really like when they text me on WhatsApp with a photo of what they are seeing on the microscope because at least I think 'okay, we are connected in this moment'. [laughs] But that is why I particularly like to do microscope-related experiments. Of course, I'm totally unable to run a project from start to finish, but I try to keep a few experiments to go to the microscope by myself at least once a month. I tend to use these experiments to test a new hypothesis, a new tool or an approach to decide if we should implement it. And I like to do fly work. I find it chilling to play with insects. Once in a while, I do some recombinants that someone needs for a project, so I can just hang out with the people in the fly room. I like it.

What is the best science related advice you ever received?
As I mentioned before, the PhD programme I attended (GABBA) had a strong impact on my decisions and I think the best advice that was given to me was by the mentor of the programme, Maria de Sousa, who we recently lost. She was really the person who pushed for this mindset that we should be free and follow our curiosity. I know that curiosity-driven research does not suit everybody, but for me it fits perfectly; it's easy to have fun in the process and to feel motivated all the time. I feel like when I was a child, when I was curious about the ants. There are other points that I learned from my supervisors, Daniel and Claudio. They always try to bring the findings into the big picture and they are great storytellers. So I learned the importance to turn experiments into a good story. Someone also told me that you should take the necessary time to think about the simplest experiment to test a hypothesis, instead of starting with a very complex one. I really liked this advice, because I tend to prefer to be reductionist and to do simple experiments. I think I get more robust conclusions through simplicity. I also think that people tend to like the advice that suits them best. [laughs]

What is the most important advice you would give to someone about to start their own lab?
The lab is about researchers, so it is somewhat common sense that you need to invest a lot of time in recruitment. But more than recruitment, it is really important that you know your lab members and make sure they enjoy their research as much as you do. So you should take time, not just to recruit them, but also to get to know them. I read somewhere the other day that you are only as good as your best postdoc or PhD student. And I totally related to that. You are competitive if you create a positive environment where people can work hard and show their talent.

Given the recent circumstances, how did you and your lab cope with the lockdown due to the SARS-CoV-2 pandemic?
Well, we coped. The i3S was, in fact, one of the first institutes to close because we had a positive Covid-19 case there. By the second week of March 2020, we had already closed. We put all the experiments on hold. The PhD students and MSc students were trying to advance with the writing of their thesis, and we had quite a bit of data to quantify, as we get a lot of microscopy data. We were having meetings every week and journal clubs. We had a plan. But that was it – we just tried to use our time as best as possible. I was trying to coordinate the team as best as I could. But eventually you need a routine. And grant deadlines approach. And a paper in revision. Thankfully, we already had some of the data the referees enquired about so we were just a bit delayed. We were also allowed to go one at a time to the institute to 'flip' our flies. It was more difficult psychologically. For me, working at home was incredibly difficult. I felt my productivity was really low. The first two or three weeks were totally chaotic. Then my partner, Filipa, and I started to create routines. We shared a calendar to organise ourselves with our childcare and household tasks. In that sense, I can't complain too much.

> **"I think it's a great job to be a scientist, and it is great to be a scientist and a dad at the same time."**

What are your views on the feasibilities of being a good parent and a good scientist?
I don't think there is any conflict between being a good parent and a good scientist. I think you have to find your work–life balance. It's really important to define your priorities in life. Of course, sometimes you have to sacrifice some of the time you spend in the lab or you have to sleep less. In fact, as a scientist, you are so curiosity-driven that your child will want to hear all about it. You can be a very effective parent, teach and transmit important values. You just need to find the time to be with your kids. I understand that sometimes we can have crazy working hours. My partner is not a scientist, so she somewhat gives me the fine touch of 'reality'. She also helps me a lot; when I have difficult times, such as a crazy grant application deadline and I have to spend all night working on it, she doesn't come in the morning and say "wake up and take your kid to school". We try to help each other and then I try to compensate in other ways. I think it's a great job to be a scientist, and it is great to be a scientist and a dad at the same time.

Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?
If you want to know a fun fact, I can share something from my past. I played the drums in a band when I was young. We're talking about the late 90s. We were influenced by grunge and played original songs in the style of Nirvana, Pearl Jam, Soundgarden and Stone Temple Pilots. It was really a fun period. I had the long hair, flannel checked shirts and the black skinny jeans to match. I was also into heavy metal and trash metal, like Sepultura and Ratos de Porão, so the style fit both. [both laugh] Unfortunately, it came to an end when I developed tinnitus and I never played drums again. I don't think I

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would be able to have a career in music anyway. Luckily the tinnitus faded and I still got to have my moment in a band. This seems like another life to me now.

Eurico Morais-de-Sá was interviewed by Inês Cristo, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.