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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Adrian Saurin

Adrian Saurin graduated from the University of Leeds and moved to London for his PhD at King's College in the laboratory of Michael Marber at the Department of Cardiology, working on protein kinase C (PKC) and stress-activated protein kinases (SAPKs) in the heart. Adrian then joined the laboratory of Peter Parker at the CRUK London Research Institute to further work on PKC regulation before becoming interested in cell division and the cell cycle. In 2008, he moved to The Netherlands for a postdoc with Geert Kops at the University Medical Center Utrecht on the functions of protein kinases during mitosis. Since 2013, Adrian has had his own research group at the University of Dundee, where he studies the spatial regulation of mitotic signalling networks with the support of a Cancer Research UK (CRUK) Programme Foundation Award.

Adrian Saurin

What inspired you to become a scientist?

I was very interested in research and my dad had a lot of heart-related health issues, so I wanted to do a project in that direction and found a lab that worked on signalling in the heart. There was no history of science or research in my working-class family. My dad was a bus driver and my mum a receptionist. However, both are into the questioning of things. My dad is a perfectionist as well – he builds model boats. So as a kid, I used to take things apart and I was always trying to find out how they work. But there were no footsteps to follow as such.

You worked on protein kinase C (PKC) in myocytes for your PhD and then on its biochemical regulation for your postdoc with Peter Parker. However, you then switched to cell division and the cell cycle – how did this come about?

I joined Peter's lab with funding from the British Heart Foundation to understand the basic biology of PKCε and spent years on biochemical approaches that didn't work. Then, I stumbled on a role for PKC in cytokinesis and that was when I started doing microscopy. I instantly knew, as soon as I started looking down the microscope and seeing cells divide, that this was what I wanted to do. At that point, I was probably six years into my postdoc and I had just discovered my way. So after we published a nice story on PKC in cytokinesis, I wanted to start my own lab.

But that's not what happened

I applied for a career fellowship from the Medical Research Council (MRC) to go to Dundee and work on mitotic kinases that hadn't yet been well characterised. I knew a lot about kinases and worked on mitosis, so I went to the MRC interview and thought it went really well. But I didn't get the position – the feedback was that I had never been in a cell cycle group and that I had naïve ideas. It felt like the worst thing that had ever happened to me. I had six weeks left of my postdoc salary at this point. My wife has family in Scotland and we thought that we'd be moving there. Instead, we had only a couple of weeks left to decide what to do next in our lives.

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You then joined the laboratory of Geert Kops in Utrecht in The Netherlands for a second postdoc

Geert gave a fantastic talk on mitotic kinases in London only a few days after the bad news. I went to speak to him afterwards and asked for advice on what to do, as I felt I had tried to set up my lab in this area and was then back to square one. He offered me a position in his lab but I hesitated because I initially didn't want to do another postdoc and my wife would need to find a job outside academia. Geert just convinced me that it would all work out – his typically relaxed Dutch style can be very convincing! Six months later and I knew how important this opportunity was. We were three labs and about 40 people in lab meetings and I learned so much about the cell cycle in Utrecht. Afterwards, I looked back at my proposal, and I realised the MRC were right to not fund the project – the ideas I had were really naïve. I had planned to focus on small niche kinases when there were so many unanswered questions about the big ones. Without a doubt, getting turned down by the MRC was the best thing that has ever happened in my career so far. It's funny how something that was absolutely devastating at the time can turn out to be so important.

What challenges did you face when starting your own lab in Dundee?

After my time in Utrecht I had about eleven years of post-PhD experience, so I wasn't eligible for most fellowships. On a side note, I'm really glad to see that funders like the MRC are now removing

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Adrian with family outside of the new V&A museum in Dundee.

age restrictions. It's important – not everyone fits in the same box and people can have good reasons to take longer with their postdoc. So after I started my lab, I didn't get any additional grants initially. I decided to work full-time at the bench like a postdoc for months. This is not a bad thing as a new group leader. You can be in control of your own destiny for a while. Just sitting in your office and trying to write grants – I've seen people making the wrong choice. In the end, we published our first paper and then got new funding from CRUK, for which I am really grateful. However, it did come down to this half-an-hour interview. It's kind of funny that you can have 17 years experience in academia and then a lot comes down to these little defining moments like interviews when things can go right or wrong. It's hard to get away from because it is a competitive field – loads of people do brilliant stuff and it's just difficult to fund everybody.

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What questions are your lab trying to answer just now?

We are trying to move away from a reductionist approach to cell biology. Mitosis is probably one of the most advanced fields and we know its parts well. The aim is to combine cell biology with mathematics to understand how these parts work together as networks. We work on the kinetochore, and it's a beautiful structure; you have all these signals that converge onto this very small space on chromosomes and it's incredibly complicated. We're interested in kinase–phosphatase integration because it's far too simplistic to just look at these as enzymes as antagonistic. Yes, they switch molecules on and off. But that's just a binary switch, and biology requires signal responses to be far more complex than that. For every molecule, there are thousands of copies and how those copies behave in time and space determines the response. For example, you can have amplitude, you can have certain localisation effects and you can get complicated response patterns, and there are many excellent examples of these in mitosis. Kinases and phosphatases work together to define how those many copies behave in time and space, which ensures that the response isn't just binary. That's a really important distinction, and that's what we're working on at the kinetochore. How will these different signals combine in a way that gives you the right output?

It sounds like the ability to combine thousands of binary switches together in different ways can lead to very complex outputs

Yes, absolutely. But complexity can also arise at the level of a single switch. If you take all phosphorylation sites ever identified – there are half a million of them across species – it still amazes me that there is one property common to every one that we know almost nothing about: the rate that phosphate cycles on and off. We are actually almost oblivious to this, because whenever we measure phosphorylation levels, we fix a state, be it through mass spectrometry or immunofluorescence or biochemistry. For a protein at 50% phosphorylation, is it that 50% of the molecules that are stably on and 50% off, or is it 100% that are flashing on and off really quickly or at different rates? We know almost nothing about these dynamics and so we make very few predictions about them. We're investigating this further because they could be very important for signal responses. They are also a beautiful example of kinase–phosphatase cooperativity at its most fundamental level.

I noticed that you also recently made science outreach efforts through an online game?

Oh yes, The Enemy Within (can be found at https://www.saurinlab.com/the-enemy-within-1)! I went to a networking event by Scottish Crucible, a great gathering of new group leaders from all across Scotland and from different fields. Abertay University is well known for their computer gaming industry and I started discussing with Robin Sloan how computer games can be used in education. I feel obliged to get messages across to the public about what we do and why we do it and I thought maybe we can get the message across to teenagers about why smoking is bad for you and what causes cancer. The problem I see is that we can all visualise that a narrowing artery may become a serious event at some point – angina or a heart attack. But when it comes to cancer, the average public knows without a doubt that smoking is wrong, but can they make the connection in the same way they do for fatty food and heart disease? It's really simple; it's damaging mutations and it's a progressive disease. Mutations accumulate in cancer just the same as an artery gets narrower and narrower. The idea of the game is that we try to show that bad behaviour can lead to cells becoming aberrant and how those progressive changes can ultimately lead on to cancer. By visualising this ongoing process, we hope that people maybe more likely to make the right lifestyle choices early in life when they can have the biggest impact.

Having established your lab now, are the challenges that you're facing different today?

One thing that struck me straight away and that I wasn't expecting was the personal aspect of managing people. I'm fortunate to have a great group working with me, but they are all individuals with different strengths and weaknesses. That's only natural. Seeing it from the other person's point of view and really trying to provide an environment that helps everyone is the real challenge. But it's also one of the most fun aspects of having a lab –very challenging but also extremely rewarding. Now, I'm at a point where we've got lots of stories to send out and we have a few in the pipeline, so it's going really well. Until recently, I didn't want to expand past a group size of five or six to really make sure that everybody gets the right conditions and a lot of time. But now is definitely the time to expand, so the next thought is how to keep things working as well as

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they do now and still expand the group. The lab is much more experienced now, so I hope this will be a natural transition.

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What is the best science-related advice you ever received?
I took advice and elements from all of my mentors. You just soak up things like how they manage the lab or the questions they ask or how they deal with issues. When I joined Dundee, Tim Newman, who was Professor of Biophysics at the time, had a massive influence on me. He reassured me not be afraid to think big but to keep things simple as well. Big and simple is a hard combination, but we should always strive for it.

What is the most important advice you would give to someone about to start their own lab?
It's really important to focus on the people in your lab. If you spend a lot of time thinking about the people and what they need to succeed, then the projects will look after themselves. For the research questions, I'd say you need a mix of big ideas and projects that are safer. However, identifying your research questions requires a lot of thought; not just with regards to why they are important, but also why you are the right person to do it and why no one's done it before. If you can identify clear reasons for this then you're probably on to a winner.

How do you get the most out of the meetings you attend, particularly in the early stages of your career?
At all stages of my career, conferences were about having fun, experiencing the science and getting to know people. It's important to advance ideas, to get advice, to listen and to learn. But it's also about meeting people. It can feel daunting at first but just be yourself and have fun. Then you can form relationships with people that you like and trust. It's important, for collaborations in particular, to feel like you can connect on a personal level.

Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?
I'm a massive Liverpool fan and their manager Jürgen Klopp is my hero. I aspire to be like him [laughs]. If I could manage my lab anywhere near as well as he manages his team, I would be really happy. He doesn't take himself too seriously, has fun and it rubs off on other people.

Adrian Saurin 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.