

## Cell scientist to watch – Steven Spoel

Steven Spoel graduated with a master's degree in biology from Utrecht University in the Netherlands before moving to Duke University, Durham, NC, for his PhD with Xinnian Dong. There, he worked on plant immune response pathways. In 2008, Steven moved to Edinburgh, UK, to work with Gary Loake with the help of an EMBO Long-Term Fellowship and a Netherlands Science Foundation Rubicon Fellowship. In 2010, he set up his own laboratory in Edinburgh as a Royal Society University Research Fellow. He has been awarded a BBSRC New Investigator Award and an ERC Starting Grant, and has been the recipient of the New Phytologist Tansley Medal for Excellence in Plant Science (2009) and an Early Excellence in Science Award from the Bayer Foundation (2013). Steven's research group studies the regulation in gene expression in response to pathogen attack and oxidative distress, in both plant and yeast cells with a particular focus on how transcription factors themselves are controlled in these processes.

### What inspired you to become a scientist?

It all started when I was a very young child. My parents were so kind to give my brother, my sister and me a patch in the garden we could tend to ourselves. I really enjoyed that – I loved working with plants, seeing them flower and so on. And while my brother and sister may have enjoyed it, they did a lot less with their little plots and it didn't take long for me to take over those plots. It was at this point – trying to grow all sorts of things – when I realised that I was very interested in plants and living things in general, and this put me on a path towards biology, even at an age when I didn't really know what biology even meant.

### What questions are your lab trying to answer just now?

We focus on elucidating the process of transcription, in particular how transcription factors control gene expression, and we want to go beyond the simplified dogma of transcription factors only binding to gene promoters to turn on or off transcription. We'd like to see how transcription factors are themselves regulated, and how their transcriptional potency is regulated. For those kinds of question, I think, the plant immune system is an excellent model because activation of plant immunity is associated with rapid changes in thousands of genes across the genome. Similarly, we started to work with yeast, where we look at oxidative stress and starvation responses, which are also associated with changes in hundreds of genes, also occurring quite rapidly. Therefore, understanding changes in transcription factor behaviour is the main focus of the lab and, within this, we specialise on two post-translational control mechanisms of transcription factors that – we have determined – are very important. One mechanism is redox-based modifications of transcription factors that, we've shown, regulates their activity and localisation and, in some cases, DNA binding activity. The second is ubiquitylation, which promotes or represses transcription factors and, thus, we're very interested in analysing how modifications by ubiquitin change their transcriptional potency.



Steven Spoel

### Do you feel that, on occasion, there's a barrier between plant and animal model system researchers? How much do you set yourself purely in the plant world and how much influence do you get from other systems?

I agree that sometimes there seems to be a virtual wall between plant and non-plant scientists, but both fields can learn from each other and did so in the past if you look at it from a historical perspective. In our studies we don't see this as a limitation. We get a lot of influence from non-plant models and the kind of work that we do transcends those traditional boundaries of plant and non-plant research. As I said, we're trying to encompass other models within the lab, albeit at a slow pace – but we're getting there and that's important because it allows us to ask bigger questions. We subsequently want to ask 'is a process we identify in one organism true throughout Eukaryota?'. And I think that's a question that should, perhaps, be asked and answered more often than it currently is.

### What has been the most influential publication or work in your field recently?

The revolution in microscopy, in particular I'm thinking of cryo-electron microscopy here, has opened up a whole new suite of possibilities for studying the proteasome. What I also find really inspiring is single-cell work, next-generation sequencing on single cells but also single cell observations of transcription. This is something we are trying to advance in my lab. I think we can learn a lot

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Steven demonstrates an arm bar technique on his student Vincent while teaching Judo.

more when we look at single-cell processes and take away a lot of the stochasticity that exists when you observe populations of cells. As plant scientists, we often look at responses in tissues, so you are already looking at many different cell types during such a response. And at the organismal level, looking at individual plants offers a whole new influence on our data because they all have different cell types as well. Understanding differences among cell types is something that, perhaps, we don't address enough in plant science yet.

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

It was a pretty steep learning curve and somewhat harsh transition. I only spent two years as a postdoc, which is a fairly short amount of time, so there was a lot to learn when I started. Also I had funding for myself, and some lab consumables and equipment, but not for staff positions in the lab. It therefore took a fair amount of time before I got a team together and the lab running, so that I could say it functions well and we have good output.

### **“As a group leader you need to assemble a team that works well together [...]”**

#### **What characteristics do you look for when recruiting new group members?**

Of course you're looking for excellence in thinking and in the science somebody does but then, for me, a key aspect to look for is whether this person is a good team player. As a group leader you need to assemble a team that works well together; if you recruit someone who doesn't function well in a team, this affects everyone and the output of the whole team could go down. In such cases, I think it's best not to hire that person, even if their scientific CV is excellent.

#### **How are the challenges that you're facing now different?**

I think the challenge for the next couple of years is the funding environment in the United Kingdom. There are some clear trends going on, at least within plant science: we're moving away in terms of funding from a lot of fundamental and applied plant science and towards translational plant science. Translational science is essential, but it should not come at the cost of either truly fundamental or applied plant science. Most of the research in my lab falls entirely within the fundamental research area and we're very concerned about future funding. Brexit, in particular, may mean that we could be facing a

situation where we're no longer eligible for funding from the Horizon 2020 program or any subsequent program. Our lab and many other fundamental UK plant science labs are being funded by the European Research Council at the moment, and that's a big point to address with Brexit around the corner – how can we fill that gap, should that kind of funding fall away and what can our funders within the United Kingdom do about this?

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

It's important to find the right balance. Of course I worked many, many hours and late nights during my PhD and postdoc years, but I think I still found a very good balance then with other things to do – it's important because it can really enrich you in ways that are perhaps completely unexpected. I was very involved in doing Judo while I was in the United States and, in fact, had my own school at Duke University and I took my Judo students to tournaments. This was a really enriching environment for me: you get to know a lot of people, but also you learn to deal with a lot of different personalities and have to get them together in a team. Subsequently, I discovered that this is a very useful skill to have when you set up your own lab – an unexpected bonus!

#### **Are you still doing experiments yourself?**

Less and less, I must admit, but I always try to do a little bit of bench work – nowadays it comes more in bursts as, depending on administrative or teaching duties, you might find more time during a certain period in the academic year. I think it keeps me in touch with what exactly my team is doing in the lab and the timescale experiments can be done in. I try to contribute to developing techniques for the lab, to set up something that my staff and students can subsequently use.

#### **Is there a technique in particular you are currently working on?**

Not at the very moment, unfortunately, but one of the last things I did was to look at ways to detect redox-based protein modifications without having to denature proteins, which normally is a required step. By not denaturing proteins, it allows you to do many more enzymatic assays to detect the addition or removal of redox modifications. We've published one way of doing this, but I was hoping to develop that further. A challenge in this method is that cells – particularly plant cells – have very high amounts of antioxidant molecules, which of course will automatically remove redox modifications. You have to prevent this from happening as soon as you break a cell open. I think if the technique works, we would be able to detect a lot more redox-modified proteins than we currently do, and that's true for all eukaryotic systems.

### **“[...] in order to get beyond incremental advances, one needs to continuously move from one large challenge to another [...]”**

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

To focus on larger research questions that are worth working on. Sometimes it's tempting to stick with a big question that you've addressed and to start answering smaller questions around it. This is of course also important to do but, in order to get beyond incremental advances, one needs to continuously move from one large challenge to another, and I think that's something I got from

my supervisors: think big, try to tackle questions that are really worthwhile, no matter how hard they are.

**What is your advice on establishing good collaborations?**

As you get trained during your PhD and postdoc, it's important to establish a network around yourself. Try to meet people in the field; I'm not just talking about people who are already at the top of the field, but anyone working around you can become very valuable to have a good relationship with. For example, Yasuomi Tada (Nagoya University, Japan) and I used to work together in the lab of Xinnian Dong and now collaborations between our labs come so naturally to us because we know each other so well and have built up trust. It's actually the same for other people we collaborate with: it's often people that you've met throughout the years, not necessarily as a group leader, but even from before.

**How do you get the most out of the meetings you attend, particularly in the early stages of your career?**

To be open and a little bit bold probably are important. You shouldn't see any obstacles to speak to somebody at a conference.

In the end, that's what conferences are for. If you feel you need to meet someone at a conference who will benefit from hearing about your work or vice versa you should, by all means, go and talk to them. That's one thing I've done throughout my career – I never hesitated to try to speak to someone and to try to be helpful.

**Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV? Are you still involved in teaching Judo?**

I used to commute between Glasgow and Edinburgh, which took up a lot of my time, but I've recently moved to Edinburgh, so I'm definitely looking at picking up Judo again. Being a coach for people and, thus, being responsible for a team was something I really enjoyed in my spare time. And now that I moved house I have got a big garden again, so I might go back to my childhood memories of fondly growing plants in the garden.

Steven Spoel 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.