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CELL SCIENTISTS TO WATCH

Cell scientists to watch – Ondřej Štěpánek

Ondřej Štěpánek is a Group Leader at the Institute of Molecular Genetics (IMG) at the Czech Academy of Sciences, Prague, Czech Republic, where he also completed his PhD. After his PhD, he spent four years in Switzerland as a postdoc in Ed Palmer's lab, and was then was awarded an EMBO installation grant in 2016 and returned to the IMG to start his own lab. His research focuses on the fundamental biology of T cells and their functions in adaptive immunity. We caught up with Ondřej to find out more about his research, the transition to group leader and his love of carnivorous plants.

Ondřej Štěpánek

What inspired you to become a scientist?

I have always been fascinated with nature and life. As a child, I enjoyed observing animals, such as ants. We also had a very simple microscope at home, allowing me to watch small creatures living hidden all around us. This is why I decided to study biology, to somehow try to understand mechanisms of life. I think this was the major inspiration, but my parents are also scientists, so they were another source of inspiration for me. Although they never pushed me to become a scientist (my mother actually wanted me to be a clinical doctor), I was born into that scientific environment, with both my parents being physicists. In fact, they are both professors at the Charles University in Prague!

In your master's degree, your research was conducted in yeast cells, and you then changed the focus of your research to immunology for your PhD – what prompted this change in fields?

It didn't really feel like changing fields, because at the end of the day, it's all biology and a lot of the things I learned working with yeast I used later on in the mammalian systems. But I decided I wanted to study what I would describe as more biomedical research; I wanted to move into mammalian cell biology. Then, I ended up in an immunology lab mostly by coincidence; I was not aiming for immunology in particular, but I was looking for an interesting project in a lab focused on molecular and cellular biology of mammalian systems. I also liked my supervisor, Tomáš Brdička, and that definitely helped. But I do find immunology fascinating. Firstly, from a biomedical perspective, because the immune system is very important in infections, vaccinations, cancer etc., and there are also diseases connected to errors in immunity, such as autoimmune diseases or allergies. Secondly, from a biological perspective, it is very interesting because the interaction between pathogens and immune systems is one of the driving forces behind evolution, and this can be studied on the molecular, protein, cellular and organismal level to find out how and why particular mechanisms have evolved.

You then moved to Switzerland for a postdoc in Ed Palmer's lab at University Hospital Basel, where you began working *in vivo* with mice to investigate T cell activation. How have you found working with multiple research models?

I would say I had it pretty nice because I started with yeast, which are unicellular, relatively less-complex organisms, and they are easy to handle and genetically modify. And then during my PhD, I worked mostly with cell lines, which was a bit more complex and difficult, but still relatively simple compared to doing experiments in animals, which I did during my postdoc; there I began doing experimental immunology using mouse models. I have now taken this further, and we are even trying to do a little bit of research with patients, for which we have some collaborations with hospitals too, and this adds another layer of complexity. Although I didn't plan it from the beginning, I have ended up on a trajectory from the simplest models to working with the most complex models, which has been quite nice.

In 2016, you then started your own lab at the Institute of Molecular Genetics (IMG) at The Czech Academy of Sciences. I understand you also completed your PhD there; what made you decide to return there to begin your journey as a group leader?

This was actually somewhat of a coincidence; it's very difficult securing an independent position, and it just so happened that when

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A lab barbecue on a rainy day.

I was looking for an independent position, there was an open position here. And I needed to find somewhere with very good animal facilities, as well as a transgenics unit and flow cytometry facilities, which IMG was able to offer. Coming back to a familiar place also made it more comfortable, knowing the institute and some of my colleagues that were still here when I returned. We also enjoy having our extended family nearby.

How did you find the transition from postdoc to group leader? Do you have any best or most challenging moments?

I think everybody who has started their own lab somehow remembers the very first weeks or months, when there is an empty lab and there is no one. Then suddenly, the lab members are starting, the equipment is coming, and you can do your first experiments; it all happens very quickly. So, it's a memorable period of life. What was most difficult for us, and most important, was acquiring money and people; if you want to run a group, you need good people and a lot of money, so this is always challenging, and I was lucky that I was able to secure pretty good funding at the beginning, so I was able to hire a few people from the outset to start working on the projects straight away. There are of course also the ongoing challenges of being a group leader, like the paperwork, managing and training people in the lab, writing grants etc., and these are all ongoing, so you have to have resilience.

Then, I think the really rewarding moments are connected with the science, for example when you've had your first paper published as a group leader. I also like the moments when somebody in the lab makes a very interesting observation, and we can discuss that and think about what it tells us about how the immune system works, or how the cells work. The other rewarding part is when students graduate, because you can see how much they have learned and grown as scientists – it's a huge milestone. Similarly, when graduates or postdocs move on to a very good lab, although it's sad to see them leave, it's great to see what they have achieved.

"I think the really rewarding moments are connected with the science"

What are the main research themes of your lab? What questions are you trying to answer?

We are mostly focusing on the fundamental biology of T cells, which are an important cell type of the adaptive immune system. Here, we are focusing mostly on two sets of questions. The first is related to signalling, because the cells of the immune system have to communicate with each other, and T cells receive signals from antigen-presenting cells. So, we want to understand how these signals are transduced in T cells and identify the molecules that are important for the antigenic response. We are also interested in signalling pathways that are triggered by T cells in these interacting cells; for instance, one type of T cell produces interleukin-17 (IL-17), so we are also focusing on IL-17-induced signalling in recipient cells. Secondly, we are investigating the diversity of T cells because these cells come in many flavours, each with quite different functions. So, you can divide these cells into many different groups based on their function (e.g. cytotoxic T cells and helper T cells), as well as further subtypes. It's very complex, and so we are trying to understand the diversity and functions of these T cells and potentially uncover novel subtypes. And we now think that we have captured a unique stage of early activated T cells, which has not been described before, which might help us to address this question of how T cells can become effector or memory T cells. So, we have these two main aspects that we are approaching from both a molecular and cellular focus.

How involved are you in the lab? Are you still doing experiments yourself?

Unfortunately, I'm not doing experiments anymore. I think the last time I did some experiments was last summer, but it was only a little bit. As the number of people in the lab increased, I just didn't have time for the experiments myself. I also don't think it's very efficient, because I think everybody in my lab can do the experiments as good as I can, or even better. I have to spend my time on other things like mentoring other people and, of course, lots of administration. When I was in the transition from postdoc to group leader, I didn't think I would miss performing the experiments, but then I realised that lots of things I have to do now are much more boring than experiments!

I understand your lab uses both *in vitro* and *in vivo* models, varying from live-cell imaging to mouse genetics and single-cell RNA sequencing. Which of the techniques you use do you think are the most challenging and/or most exciting?

What is most important is the combination; there is power in combining systems biology or single-cell RNA-seq data with reverse genetics models or disease models, for example. In terms of difficulty, the transcriptomic data is challenging, because you need people who can not only analyse it, but also interpret it. And there is usually a big war between the biologists that have the biological questions and the information that can be extracted from the data, but they cannot efficiently use the data to answer all their questions. Fortunately, in addition to the great team performing wet experiments, I have at least two people in the lab who analyse this large data, one of whom, Juraj Michálik, is a computational biologist, and the other, Veronika Niederlová, is a student who is able to connect these two fields. I think it is really important to have

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a dialogue between the people that understand the data and understand the biology.

What elements, inside or outside the lab, have been key to your success so far?

I would say being opportunistic and improvising; you cannot always plan for everything and follow other people's advice, as every situation is unique. Additionally, it's a bit more difficult in Central and Eastern Europe, as scientifically, it is under-developed still, compared to places like Germany or the UK, where there are more funding opportunities. So, I think it's important that everybody finds their own way; I don't think there is one set of rules that you can give to everybody who is becoming independent. In terms of research, I think it is important to have good people on your team and a supportive environment, both of which I have here at IMG.

"...it's important that everybody finds their own way; I don't think there is one set of rules that you can give to everybody who is becoming independent"

I see you are active on Twitter: what are your views on social media for scientists?

I find social media useful because I can learn quickly about papers that are published; it's like an instant Table of Contents, as the papers come out, people are tweeting about them. I also use it to share our work on Twitter when we have something published. And, of course, I use other tools like PubMed searches, but this can sometimes take longer and I don't have anything like that for BioRxiv, for instance. I think it's also a good place to read and learn about scientific policy issues, which people like to discuss on there. So, it is useful, although I would not overestimate it, as traditional journals are still the major platform for scientific communication.

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

One hobby I have is that I grow carnivorous plants; I actually have some of them in my office, which has become a bit of a garden, and I have some more at home. This is something I started as a kid; I am fascinated by carnivorous plants because it's funny that usually animals eat plants, and then there are these plants that can eat animals. Some people even research these plants, so I sometimes read papers about the mechanisms they use and adaptations they have.

Ondřej Štěpánek was interviewed by Daniel Routledge, Cross-title Reviews Editor at The Company of Biologists. This piece has been edited and condensed with approval from the interviewee.