© 2018. Published by The Company of Biologists Ltd | Journal of Cell Science (2018) 131, jcs227223. doi:10.1242/jcs.227223

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Tobias Zech

Tobias Zech studied biochemistry and received his Master's degree at the Freie Universität (FU) Berlin, Germany, before moving to the University of Oxford, UK, for a PhD in the laboratory of Thomas Harder on T cell receptor signalling and activation. In 2008, Tobias joined Laura Machesky at the Beatson Institute in Glasgow for post-doctoral work on cell migration and motility and the role of the actin cytoskeleton. Tobias established his research group in the Department of Cellular and Molecular Physiology at the University of Liverpool, in 2014. There, his group studies processes of cell migration and cancer cell invasion, with an emphasis on actin dynamics and receptor trafficking.

Tobias Zech

What inspired you to become a scientist?

That is a question my parents ask a lot as well! Neither of them have a scientific or medical background. I was, however, the cliché kid-with-the-chemistry-kit. My friend, the neighbour's kid, even had a dedicated room in the cellar for chemistry and science kit stuff, and we spent a lot of time there. He's now a medic and I went on to study biochemistry…

How did you enter the immunology field during your biochemistry studies in Germany?

We were able to do many different practical courses to get credits. One of them was in nuclear magnetic resonance, and the project was about the binding of novel proteins to the T cell co- receptor CD2. I guess one thing then led to another: in my last year of studies, my supervisor Christian Freund (FU Berlin) put me in contact with his mentor Ellis Reinherz (Dana Farber Institute, Harvard Medical School) who is an immunologist. I went there to start my diploma thesis and to work on CD2 binding proteins, and that's how everything developed.

What questions are your lab trying to answer just now?

We would like to understand the molecular mechanisms that drive invasive cell migration in a 3D matrix environment. What enables cells to move through these environments? In particular, we are interested in the role that tensile force gradients in the actomyosin network have in establishing nuclear force coupling – the nucleus is one of the biggest roadblocks to any efficient cell migration, given its size. Furthermore, what influence do force gradients have on the front–rear polarization of the cell? We analyse this by looking at how forces are applied on adhesion complexes, how their composition is changed, how forces are applied on the nucleus. Others and I have developed force biosensors that can measure forces applied on the nucleus, and how they spatially correlate with motion when stress is applied to the matrix around them. We are also looking at how polarised physical transport, in particular endosomal transport, is regulated in cells. What is the interplay of actin-mediated recycling or salvaging of trans-membrane proteins in the endosomal system, and the ubiquitin-mediated sorting towards degradation through the ESCRT complexes? The final thing we are currently looking at is the influence of the actin cytoskeleton and, in particular, the Wiskott–Aldrich syndrome protein and SCAR homolog (WASH), an actin polymerization complex, on microtubule dynamics. WASH is an endosomal factor but is also associated with centrosomes. It seems that actin polymerisation and microtubule dynamics are linked in ways we are only beginning to understand.

3D cell systems and their environment are, of course, very complex. How do you address sample heterogeneity and reproducibility when quantifying data?

This is definitely something that we care a lot about: image resolution and imaging frequency, signal-to-noise ratios – when we use the force biosensors in a 3D matrix, it can be tricky. We've also developed mass spectrometry approaches that enable us to look at protein complexes in a 3D matrix. This is to make sure we have very different approaches because, I think, one has to be very careful with the interpretation of data. I have recently been asked why we still look at 2D cell systems when we want to understand 3D, and I think it is a good thing to compare results. If you have new results, go back to a 'simpler' system and test them. Reproducing the data and robustness of the system are definitely aspects we frequently think about.

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

I wouldn't want to single anyone out, because there are so many papers that influence you and certainly for very different reasons: some studies are very rigorous and might give you a very solid basis for interrogating everything. They might not show the most ground-breaking new discovery but you find yourself looking at them every week to see how the experiments were done. Then there are papers with really nice and

Tobias Zech's contact details: University of Liverpool, Institute of Translational Medicine, Cellular and Molecular Physiology, Liverpool L69 3BX, United Kingdom.
E-mail: T.Zech@liverpool.ac.uk

Journal of Cell Science (2018) 131, jcs227223. doi:10.1242/jcs.227223

Family fishing time in the Scottish Highlands

thought-provoking hypotheses that inspire you to say 'oh, maybe that's something we can build on'. I always get influence from many different directions.

"Don't wait for applications; […] go to people and ask them if they are interested."

What characteristics do you look for when recruiting new group members and composing your team?

What I did – and hopefully still do – is to try and approach people directly. Don't wait for applications; at conferences and at the University, go to people and ask them if they are interested. Strike up conversations and get to know people already. Regarding the composition of the research group: I like to have teams that work on the same subject field. For example, two people will work on nuclear force transduction and invasive cell migration, with separate projects but complementary skills that can enhance each other's work.

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

It is a very interesting and challenging experience to start from scratch and to purchase equipment. I was very lucky that there was a great summer student in the lab of my post-doctoral supervisor Laura Machesky. She decided to extend the Erasmus exchange and move from Glasgow to Liverpool when I opened the lab. Another PhD student who had already started in the neighbouring labs of Sylvie Urbé and Mike Clague joined quickly, so I was never alone. People had very generously allowed this student to start earlier, and this generosity and friendliness is one of the great things about the department here. So when I arrived, it enabled a 'hit the ground running' situation for me.

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

Certainly the funding situation is a big aspect at the moment. Of course, this is something that a lot of new group leaders will experience at one point or the other. I focused on publishing the first results, which we have done, and then to build on the basis of that in the next year to apply for more funding. It is a constant thought in the back of your head that you have to apply for the second round of funding after your initial funds are used up. Time goes so quickly! Luckily, we are pretty secure now.

What is your advice on establishing good collaborations?

I have always been, and I am, very excited about collaborations. In most cases they were very true to form and really are either still ongoing or the relationship remains very close. Collaborations are not only about the current project but about being able to always ask someone for reagents or advice on a project. That has been the case throughout my career. It started during my PhD when, unfortunately, my PhD supervisor had an accident and I had to go to Australia for a long time to work with our then-collaborator Katharina Gaus (Sydney), with my adviser Gillian Griffith (Cambridge) stepping in as supervisor. This led to me to have a very collaborative, open mind-set from the beginning. There's quite a bit of research output that I'm associated with as part of a collaboration.

"If people have ideas and come up with concepts, let them follow this path"…

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

I don't have specific advice that comes to mind; rather, observations from the labs I have been in or a part of have stuck with me. I thought they were very well run, and people were encouraged to be open-minded about research and given the freedom to express their own ideas. If people have ideas and come up with concepts let them follow this path; of course, give guidance but it's very important to generate a spirit of creativity in a lab. It creates a happy workplace, I believe.

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

I don't mind working long hours – a prerequisite of the job – but this does have an impact on family life and I think it is something that urgently needs to be looked at to make research an attractive career prospect, for all the hours in the lab are a deterrent to many. Some of the best young researchers leave the profession because of entirely avoidable reasons. When you are a new group leader, you have a myriad of different, constantly shifting things that require attention – and these weigh on your mind; and sometimes one can feel that the actual scientific research is gradually slipping to the bottom of the to-do list. Quite often, when you take a step back, though, you see that there actually is progress. Things are moving forward nicely if you just take away the day-to-day concerns you have. It does help to have at least one day a week away from the lab, which I also recommend to everyone in the group. Work–life balance is a very personal thing, so it's very hard to answer because everybody ticks differently. The only thing I know is that if you work long hours, or a lot of days without breaks, it hinders productivity and wellbeing.

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

I am fond of water-based activities. In Liverpool, I am thrilled to be near the coast again. I have always loved wind-surfing and surfing, though rarely find the time to do them. A relatively new pastime is fly fishing; every summer I spend a week or two standing in a river doing nothing much. And certainly almost never catching anything! That's something I really enjoy. Also, as a family, we go up to the North of Scotland and just enjoy the nature there.

Tobias Zech 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.