

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Thomas Iskratsch

Thomas Iskratsch studied food science and biotechnology at the University of Natural Resources and Life Sciences in Vienna, Austria. He then decided to pursue a PhD in cardiovascular biology with Elisabeth Ehler, in a joint venture between the Cardiovascular Division and the Randall Division of Cell and Molecular Biophysics at King's College London. After this, Thomas did his postdoctoral work with Michael Sheetz at Columbia University in New York, dissecting the role of mechanobiology in cell migration. In 2015, he returned to Europe to start a semi-independent position at King's College London. He moved to Queen Mary University of London in 2017 to start his own lab, also lecturing in bioengineering. Thomas was awarded an Intermediate Basic Science Research Fellowship from the British Heart Foundation in 2015 and a BBSRC New Investigator Award in 2018. His lab focuses on the role of mechanosensing in the development and function of the cardiovascular system, and how mechanical forces shape cell behaviour and differentiation.

What inspired you to become a scientist?

At school, I was always interested in the science subjects, especially chemistry, maths and physics. Then, after school, I had one year of national service and I worked for the Red Cross, which gave me a little bit of headspace to think about what I wanted to do afterwards. I was undecided, initially, between two big directions: I was either going into arts and design or going into research and natural sciences. In the end, I thought that the interest in science was outstripping the interest in the other direction. But the decision to actually stay in academic research wasn't clear to me at the time; I didn't know what job I would end up in. My interest in chemistry started to grow, and a friend who was studying food science and biotechnology [at the University of Natural Resources and Life Sciences] recommended this course to me. I took his advice and it was a great choice, because it involved a lot of practical courses. During one of these, you could choose to work in a research lab setting, which I did, and I got more interested in doing that type of research than the industrial work that I was doing as a part-time job for a pharmaceutical company.

How did your interest in the cardiac system come about?

I did my MSc degree project in a glycobiology lab, in collaboration with a lab at the Medical University of Vienna that had been working on muscle biology, especially focused on muscular dystrophy. There, I was first exposed to research with muscle cells and I was intrigued by how beautiful they are when you look through a confocal microscope. Everything that was related to muscle biology really caught my eye. After my MSc degree, it was a clear decision for me not to go into industry and to continue in academic research, which was so much more exciting. And I continued to work as a research assistant in the lab at the Medical University, until I moved to the UK for my PhD, so I had the opportunity to learn some skills there. I really understood that this was what I wanted to do for a living.



Thomas Iskratsch

What questions are your lab currently trying to answer?

During my PhD, I started to get interested in mechanobiology. As you know, forces are an important outcome of cytoskeleton rearrangements in general, but particularly in the heart and the cardiomyocytes. In the context of these cells, and most recently in vascular smooth muscle cells, I'm trying to understand how they interact with the environment and how they sense the surrounding mechanical properties. In a lot of cases, this depends on the interaction of various signalling pathways, either initiated by chemical or mechanical stimuli. In the heart, it's very important to look at inflammation signalling in combination with mechanical signalling. Moreover, in the vascular smooth muscle cells there are various mechanical signals, such as stiffness and blood pressure, so I recently got interested in how those different pathways are intersecting and interacting with each other.

In the biophysical research field, forces and how to probe them have always been a matter of interest. Are there any new techniques that you're adapting for your research right now?

Mike (Michael Sheetz, with whom I did my postdoctoral work at Columbia University) had a lab with great people who all worked together and taught each other different things, so I learned a lot of the intricacies of mechanobiology research. He also had a lot of tools to play with, like optical tweezers, magnetic tweezers and all

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Thomas hiking in the Austrian woods with his son Theo.

sorts of microscopes, so it was a cool playground for me to learn new things and, obviously, to learn everything about mechanobiology. Now I'm collaborating with people who develop new tools and techniques, and we are trying to adapt those for our research, including 3D *in vitro* models or DNA origami to look at different receptor ligands in a very controlled manner, and understand how those different receptor ligands are stimulating the cells. I'm also working with industry partners to adapt their equipment for our research needs, for instance, to apply hydrostatic pressure onto cells in a controlled manner. So it's a group of various approaches that we then combine with imaging and high-content image analysis, with a little bit of machine learning to look at large datasets and try to make sense of them.

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

I had it fairly easy because it was a very staged approach. Mike [Sheetz] gave me a lot of liberty and he was relatively hands-off as a PI, so that allowed me to gain some experience in organising myself. I got a fellowship [at King's College London], which was not a proper independent position, but still you get to learn how it is to have people working for you and slowly grow into it, which was great for me. I got a research assistant with that fellowship, and I was lucky to get two PhD studentships, so I could slowly transition from actively being at the bench, doing the research and doing most of the project myself, to handing work over to my students and my research assistant. By the time I got the job at Queen Mary University, which was my first independent position, I already had a small team that I could bring over. It was as easy as a transition can be, in the sense that I had funding, I had people who were already working on the project, and geographically it was a very short move.

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

There's a lot of different things. As a research fellow, you're at the bench yourself a lot and you have some people who are helping out. You don't have many administrative duties, you don't have any teaching, and you can really focus on doing the actual research. Now, I have the usual duties that come with a normal academic position and I have teaching. Obviously, you have to be more hands-off and work at a more strategic level; try out some things but let others take over and do it in their own way, and then you discuss it. You try to steer them and give recommendations and suggestions, but you have to let go a little bit and be confident that they are great people and will do great things.

Are you still doing experiments yourself?

I'm not doing full projects, but I like to do microscopy whenever I can. I like to try out new systems and new tools that we have so that I can understand their capabilities and limitations, or just get some new ideas for research and get some preliminary data for grant applications. In terms of lab work, during term time it's difficult to have a full experiment from start to finish. I feel a bit bad about asking people in my lab to start an experiment and then take it over – then it's more of a burden for them. I try to do a little bit, but mostly I go to the microscope to teach people how to do certain things, or to play around and try something new. That's my approach. But in terms of analysis, I still do quite a lot of work.

Do you enjoy teaching?

Yes, I do in general. There are a lot of different facets to teaching. I only realised when I started how hard it is to put together the material for the lectures. It took me a lot of time to do this, and that wasn't the most enjoyable part. But there are great students in the classroom who are actively interacting, and that's always quite fun. Queen Mary University is very diverse as an environment. It's good to see people who come from less-privileged backgrounds engaging and being enthusiastic; I came from a similar background, so it's really satisfying to see that happening.

Tell us about the 'Hacking Hearts' project

It's a really nice project! It came about when I was looking for an outreach activity for a grant application. For the impact statement, I wanted to go a little bit further than just social media, so I thought that it would be nice to do something in the realm of art and science. A mutual friend brought me in contact with the organiser of the arts and science course and we discussed whether there was potential to put this into the grant application. A first part of this collaboration was the 'Hacking Hearts' project, involving Central Saint Martins [University of the Arts London] and also Tokyo Tech [Tokyo Institute of Technology]. The idea was to get art students with all these different backgrounds in art, including jewellery design, furniture design and architecture, exposed to actual research about heart biology and disease, let them create artworks based on what they experience, and present their artworks to the general public in a symposium. I really liked the idea. There was a one-week workshop where, on the first day, we presented our research to the students; then throughout the week, they were exposed to different materials that they could start playing around with and start formulating their ideas. In the end, there were really amazing artworks, including performances that also involved the audience. You can see some of them on the website of Central Saint Martins (<https://www.arts.ac.uk/colleges/central-saint-martins/stories/hacking-hearts>). A social scientist was also involved who studied the communication between

the artists and scientists, and the outcome will eventually also be published as a research paper. It was a great project and, as an additional perk, the scientists also got some hands-on time, trying to make some artwork ourselves. It was something completely different to what we normally do, and I found it quite enriching.

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Do you think taking time to participate in science outreach activities should be more of a priority for scientists?

It’s definitely good to communicate what you’re doing to the general public, and try to be creative about how you do this, in order to reach out to a wide audience. I think there are lots of different ways to do this. It makes sense to find something that you enjoy doing because in the end it’s your time that you’re investing. We are mostly funded one way or another by the general public, so they have a right to know what we’re doing.

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

There are two pieces of advice. One is ‘don’t burn any bridges’, which I found great advice. I’m still in contact with my MSc supervisor and I still sometimes ask him for advice as a mentor; same with my PhD supervisor and also with Mike [Sheetz]. I often like to see different perspectives on issues. When I am interviewing for a job or when I am writing applications, it helps a lot to get different perspectives and stay in touch with people. Generally, I was lucky that I always enjoyed the environment I was working in, and always enjoyed working with my supervisors, so it was natural to stay in touch. Another piece of advice is actually something that Mike Sheetz was saying to a PhD student in the lab: ‘Grab the bull by its horns’. We all found it super funny, but it’s great advice. If you have the opportunity to do something, just do it.

Is this something that you also transmit to your PhD students?

Definitely. You need to persevere; there are all sorts of difficulties all along the way, but sometimes you just have to do it, and in the end you’ll get something out of it.

Related to perseverance, given the circumstances right now, how did you and your lab cope with the lockdown due to the SARS-CoV-2 pandemic?

It’s a tricky situation. For me, as for many other researchers with children, the challenge is to combine work and childcare, which affects work times and patterns. Sometimes it works better than other times, and it happens that my two-and-a-half-year-old son is joining in on team meetings, jumping up and down or throwing a tantrum in the background. However, I think it’s especially frustrating for people in the lab who are only in the early phases of a project. Obviously, there’s never an ideal time for a lockdown or a situation like this, but they have only limited material that they can work with or analyse, so it’s a difficult situation for them. I suggested to them that they should think about what tools they want to learn, for instance coding or trying out different software, so that they still use the time to gain something for themselves that will be useful for the project once the lab opens again.

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

I was a total heavy metal kid. When I was growing up in Salzburg, I went to see any band that would come and play metal music. I would always go with a bunch of friends, and we were always stage-diving into the crowd. One day, I was jumping off the stage and crowd surfing, but then I fell on the floor. I had really long hair at the time, so someone stepped on my hair, and as someone else tried to pull me up to help me, I lost a good chunk of hair! I stood there bleeding from my head. That was the last time I went stage-diving.

Thomas Iskratsch 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.