© 2018. Published by The Company of Biologists Ltd | Journal of Cell Science (2018) 131, jcs217372. doi:10.1242/jcs.217372

CELL SCIENTISTS TO WATCH

Interview with 2018 Hooke medal winner Andrew McAinsh

Andrew McAinsh received his PhD from the University of Cambridge, UK, working in the laboratory of Steve Jackson on DNA damage and repair mechanisms in yeast. He then joined the laboratory of Peter Sorger as a Jane Coffin Childs Fellow to work as a post-doc on kinetochore biology at the Massachusetts Institute of Technology, Boston, USA. In 2005, he returned to the UK to establish his independent laboratory at the Marie Curie Research Institute, Surrey, before moving to the University of Warwick in 2009 to co-found the Centre for Mechanochemical Cell Biology (CMCB). Subsequently, Andrew was appointed Professor of Cell Biology and became a Wellcome Senior Investigator, and was awarded a Royal Society Wolfson Research Merit Award. He co-directs the MRC Doctoral Training Partnership in Interdisciplinary Biomedical Research, and in 2017 became Head of Division of Biomedical Sciences at Warwick Medical School. Andrew is interested in understanding how the chromosomal multi-protein complex, the kinetochore, ensures error-free chromosome segregation. He is the recipient of the 2018 Hooke medal, established to recognize an emerging leader in cell biology. The Hooke medal is awarded at the annual spring meeting of the British Society for Cell Biology (BSCB).

Andrew McAinsh

What inspired you to become a scientist?

To be honest, I didn't find biology very interesting back in school – I was much more into art and design. However, I did like science per se, because it has this artsy side to it as well. Then, during my A-levels, our teacher brought some *Drosophila* stocks to school and showed us the different phenotypes, such as eye colour. He was really good and taught us everything about the antennapedia mutation and the genetic basis of it. At that moment I thought: now, that's really cool – this is something I could actually do. I guess the combination of good teaching, actual practical work and seeing things amazed me, and I decided to go to Manchester University to do my undergraduate degree. There, I started reading genetics, but as soon as I attended the courses on molecular biology I realised that I was less interested in genetics, but much more in the molecular basis of phenotypes, so I swapped my course.

Back then, it was certainly a great period to look at the molecular biology behind genetic mutations...

Yes, we had all these mutants and their phenotypes, and we were starting to see how this was working. I had a great time at university; another very important moment was the cell cycle course with Iain Hagan. He gave these fantastic lectures and would show us real data, actual research papers. A lot of students said that it was too difficult, and that they simply wanted nice lecture notes, but Iain insisted on looking at the experiments and the data. I loved it and was very keen to go to Iain's lab because I wanted to do a PhD, working on fission yeast and all these exciting new cell cycle mutants. To my surprise, Iain said 'No, you shouldn't come to my lab.' He explained that I needed to move around, to go to different places, and see different things. Iain then recommended Steve Jackson, who was building a lab in Cambridge to work on DNA repair. Steve was working on DNA-dependent protein kinases, and ATM had appeared as being a critical mediator of DNA damage signalling. This was also very exciting for me, and I joined Steve's lab in the end.

Followed by a post-doc with Peter Sorger (Harvard), and the work from your own research. Would you say that you nonetheless drifted back towards what motivated you to join Iain's lab?

Did I go 'full cycle'? Yes, I think there's some truth in that. Steve's lab was an exciting place at the time, there was just so much going on and I learned a lot. Next door, Jonathon Pines had started live-cell imaging and was injecting fluorescent proteins into live cells. I loved the look of that – to be able to look at both the spatial and temporal control of cell cycle and cell division. Peter Sorger's lab just had a paper in Cell out at that time, looking at budding yeast kinetochores, and they had started imaging the localisation patterns of kinetochores. From there onwards, they were able to identify other new kinetochore components in yeast. It was beautiful, and I thought I'd love to do something like that.

Andrew McAinsh's contact details: Division of Biomedical Science & Centre for Mechanochemical Cell Biology, Warwick Medical School – University of Warwick, Coventry, CV4 7AL.
E-mail: A.D.McAinsh@warwick.ac.uk

Journal of Cell Science (2018) 131, jcs217372. doi:10.1242/jcs.217372

Andrew riding in the Vercors Massif, France – still thinking about kinetochores….

What questions are you trying to answer in your research group?

It's a story of my interests and the constant influence of the people around me. Rob Cross next door has always been a mentor, and he's looking at single-molecule mechanics. Rob has always been keen on understanding exactly how one protein (kinesin) works in detail. I've been working on the multi-protein machinery that are kinetochores, and it just seemed like a completely intractable situation in comparison to Rob's approach. But we started thinking more and more about the kinetochore as a machinery, and its mechanics, as it needs to deal with forces and generate and sense forces. Thus, if we imagine it as a protein machine, how do the parts move, what are the requirements, how do these link to function? It's quite tough to get at, because measuring the force on a single molecule is simpler than that on a kinetochore. But now it has started to happen, and some labs have done wonderful biophysical experiments on purified kinetochore particles, for example Sue Biggins (Seattle). Again, I like that in science we can witness such things happening in the research community. Our focus therefore is on the response of kinetochores to force. How is their behaviour, their movements and attachments to microtubules influenced by this? In the end, it's about how kinetochores prevent erroneous attachments to the spindle, and thus errors in mitosis. We also work on molecular motors that are implicated in this process, but this is a side line for the lab. Again, this is Rob's influence – I always followed his single-molecule experiments and thought that was just great fun, and it's therefore a personal interest really, and a collaborative effort. The main thing for us is kinetochores in somatic cells.

You've also developed an interest in meiosis, right?

Yes, a recent effort is to look at human meiosis. Being in Warwick helps with that, because we have a reproductive clinic here, and there's the possibility to get human oocytes. We'd like to take all the tools and live-cell imaging we've developed for studying dynamics in mitosis and apply this to meiosis I and II. How does it all work and how do kinetochores behave in this? And why is there so much aneuploidy in human embryos? It's counterintuitive. Because human oocytes are difficult to work with for various reasons, the right image-analysis tools and quantitative approaches are going to be needed to make this accessible. Nigel Burroughs is our collaborator in the Mathematics department, and it's been great fun working with him on kinetochore dynamics in mitosis. To go out of your comfort zone is important in order to understand the problems you're facing, and this has enabled us to develop more advanced tools. It has also been essential for our research to have people in the lab who can do both the computing and the bench work.

> **"…I'd be hard pressed to find any paper I've ever published where one reviewer hasn't made a really good contribution to the science."**

You put your recent manuscripts on the preprint server bioRxiv. What's your take on preprints?

It's taken me a long time to do it, I have to say; I've been worrying about depositing a preprint quite a lot. Not for the reason that somebody else might see what you're doing – transparent science is great. In fact, I really value the peer review process. It's an imperfect situation and it's much talked about, but in the end, I think I'd be hard pressed to find any paper I've ever published where one reviewer hasn't made a really good contribution to the science. That's really worth something. Yes, there are issues with peer review, but we shouldn't forget that you often get some very insightful comments, great suggestions for experiments that will substantiate what you found or change the direction slightly. That's the scientific process in my view; you get to a certain point and then you try to improve and retest your ideas. Overall, the review process makes papers better. That's why I was slightly worried about putting a paper out there that had not been through that process – you find yourself worrying even more, internally, about the work.

Would you advocate commenting and reviewing on preprint manuscripts in order to make it better?

Yes, I like the idea of constructive feedback. I'm not quite convinced I'd want to conduct the reviewing process fully in public, but if somebody made some helpful comments, I would certainly be there writing back to that person. I'd go offline to have that conversation and then think about it further.

Regarding your own career: you started at the Marie Curie Research Institute (MCRI), moved to Warwick and co-founded the CMCB. Now you're Head of Division of Biomedical Sciences at Warwick Medical School and the Hooke Medal Winner 2018. How do you feel about your journey?

A lot has happened. When the MCRI closed down, there were a couple of options for what to do next; then, the opportunity arose to go to Warwick, together with Rob and Anne Straube to continue our collaborations. This was fortuitous – to have the possibility to be involved in designing the new laboratory space that we're sitting in now, and to take part in thinking about the CMCB and where it should go as an interface between cell biology and biophysics. At the time it wasn't the obvious thing to do, as there wasn't a large cell biology community in Warwick, but it was a very exciting time. Over the years, we brought people in and now we have a great research community, including an environment that is provided for the students and the post-docs.

The CMCB has built its extension in 2016, and now you have a lattice light-sheet microscope. It's certainly one of the best places to do cell biology in the UK nowadays?

Well there are brilliant scientists at several places around the UK, and looking at them I find myself thinking 'I wish I could do that

Journal of Cell Science (2018) 131, jcs217372. doi:10.1242/jcs.217372

experiment', but it's certainly a great place to come to. You can be a student, a post-doc or career development fellow and build a successful career in a great environment here. We can and want to attract more people, and one of the challenges is to expand and diversify. My job as Head of Division is also to pursue these visions now. It'd be good for Warwick; you project the science and the campus twenty years into the future, and we'd like to see it thrive.

"…identify an interesting, good scientific question and try to answer it."

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

It's to identify an interesting, good scientific question and try to answer it. It has to be tractable in your career stage – that question's different whether you're a master's student or an experienced post-doc. Then: be focused, don't try too many things at the same time; stick to your research question and have the determination to finish the project, even if it means doing all those experiments that aren't the most exciting ones in the world – all the controls and all those things that must be done and that are really important – just do them, and do them well.

Could you tell us an interesting fact about yourself that people would like to find out about you?

We have four children, and the boys are identical twins, which is really interesting. Of course, as a scientist, you look at them and you're thinking, okay, identical twins, you've got the same instruction book, and then I look at them and I'm going: no! Genetics only takes you so far! [laughs] The interactions between twins is incredible and I feel very fortunate to have the opportunity to see this happen. It's quite challenging, too, having four children. All the credit there to my wife, who's just unbelievable. And whenever there's some time left, I love riding my bike. I am happiest when I'm carving through the hairpins in the Alps or the Pyrenees.

Andrew McAinsh 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.