INTERVIEW

An interview with Kate Storey

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Kate Storey is Professor of Neural Development and Head of the Division of Cell and Developmental Biology at the University of Dundee in Scotland. Her lab works on neural differentiation in the developing spinal cord. A Fellow of The Royal Society of Edinburgh, the Academy of Medical Sciences and the Royal Society of Biology, in 2019 she was awarded the British Society for Developmental Biology’s (BSDB) Waddington Medal, which recognises outstanding individuals who have made major contributions to UK developmental biology. After her award lecture, we caught up with Kate to survey her career and hear her thoughts on the field’s future.

You’re here in Warwick to receive the BSDB’s Waddington Medal – what was your reaction when you found out you’d won?

I was surprised and delighted. It really means a lot, mainly I think because it’s given by the community and feels more special than other awards because of that. Plus, I never imagined it would be given to me!

If we go back to the beginning, what got you into science, and biology in particular, in the first place?

It all started with a lesson at school. It was early on in my first year of secondary school and in a slightly chaotic classroom with me sitting at the back and a timid but patient teacher standing at the front. She was holding up some cards showing the life cycle of a frog, which just looked fantastic. The fact that it all started with a single cell drew me in: I began wondering about how on earth that one cell would go on to become a whole animal. Where was the information and where were the instructions? That took me into thinking about how the cells become different from one another and so on. So even from the age of twelve, I was wondering about development. I think at that particular age you’re casting around for what makes sense in the world, why are we here and those sorts of things, sometimes not in a totally conscious way. I had found something that gripped me, in comparison to religion which at that age I found puzzling. The fundamentals of biology were self-evident and provable, and I was really taken by that.

And you took this love of biology with you to university?

I went to the University of Sussex and for the first two years studied biochemistry before switching to neurobiology. I became interested in the nervous system for the very simple reason that, out of all developing tissues, this is the one that ends up being the thinking part. I couldn’t quite imagine how cell specialisation ultimately led to thought.

I was taught by Brian Goodwin, a mathematical biologist and philosopher, and in my final year he introduced me to Michael Bate from Cambridge who had come to give a talk in the department. In those days, when you went to do a PhD, there wasn’t a written project – it was something you negotiated with your supervisor. And the Department of Zoology in Cambridge was an environment in which everyone was potentially your supervisor: you could seek out help and interact with anybody, and other PIs were very receptive. Essentially I was sent away for three months to find a project. Mike suggested a few things, I tried a few things, and eventually I settled on earthworm development, which surprises many people, but it was and is an incredibly intriguing system. Earthworm embryos have cells called teloblasts, which behave as stem cells, dividing asymmetrically to eventually generate the whole of the body axis. The teloblasts result from a stereotyped pattern of cell cleavage, and so you might imagine that teloblast fate reflected segregation of determinants, but previous experiments had shown that you can remove the region containing them and the embryo regulates: it just finds another way to generate its body. And of course you can just chop an adult worm in half and it will regenerate, so it’s an amazing animal for studying developmental regulation. I wanted to know what these teloblasts gave rise to: I tried to label them with minimal success, but I managed to ablate them rather efficiently. I found that the embryo compensates, but not completely, for their loss.

After my PhD I went to the USA on a Harkness Fellowship to work with David Weisblat, at the University of California in Berkeley. David investigates leech embryonic development. These embryos have massive teloblasts that really do matter: ablate those and you get big defects. I was there for a shorter time than planned.


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I was expecting our first child, Alexander, and we decided after all to have him back home in the UK.

**How long were you out of the lab after this?**
It was nearly two years. I say it was a career break but actually I was doing lots of reading, and writing and publishing papers from my PhD (which appeared back to back in Development!). And it was during this time that I realised that I really wanted to work on nervous system development, but in vertebrates. I had been told that Claudio Stern, then at the University of Oxford, would be a good person to work with, and he very kindly wrote a grant application accommodating my wish to only work half time. He was very supportive. My contract meant that I could be very productive – I did lots of experiments grafting the chick organiser region, the node. I was trying to map changes in neural-inducing ability of the node over time, even repeating some aspects of Waddington’s experiments. I would then go home and Geoff Carlson, a technician also supported by this grant, would continue the work, fixing the embryos at the right time and processing them, and it worked out quite well. This flexible approach and technical support kept me in research at critical time in my career.

**How did you find the postdoc-to-PI transition?**
After my post-doc with Claudio I was recruited as a demonstrator in the Department of Human Anatomy and Genetics in Oxford. This meant I spent three days a week in the dissecting room teaching human anatomy to medical students. I never really got used to the emotional challenge of dissecting cadavers. I was trained by the department and trained by region, so there were some parts of the body I was better at than others – and depending on which term it was I would be doing more or less time in the dissecting room. At the same time I had a lot of tutorials and lectures to deliver, it all added up to quite a big teaching commitment. But alongside all of this, I wrote grants, and when I started to get funded, my research began to develop, in large part because of the people who joined the lab. I had the good fortune to work with several outstanding postdocs: Jenny Brown had worked with Cheryll Tickle, knew the chicken embryo backwards and had thought a lot about it; Ruth Diez del Corral and Ann Goriely were both Drosophila researchers and incredibly good molecular biologists, who brought new skills to the lab. Jenny, Ruth and Ann brought expertise and commitment that I was so fortunate to have in the early stages of the lab.

**And in these early days, what were the questions you hoped to answer?**
I began by trying to continue to develop ideas around my research with Claudio, looking at the inducing abilities of the organiser, and I had some funding to do this from the Medical Research Council (MRC). But then I realised that I needed to set off in my own direction. I’d been investigating neural induction and now started to ask how the spinal cord is generated over time – how the body axis elongates. I was particularly interested in how cells retain the ability to continue to generate neural tissue throughout the elongation process. Having established that neural induction is quite an early event, the question shifted to how do cells retain this ability? Within this spinal cord primordia there are also cells that are going to make non-neural cell types, so there’s still lots of cell fate decisions being made in this cell population. We asked what tissues and signals regulated the progressive onset of neural differentiation.

In the early days it is very important to diverge from the main interests of your postdoc lab, to ask original questions. At the same time you are building on what you’ve learned, applying your technical and intellectual expertise to something new. It’s also clear that you won’t get funded to do radically new things, especially when you are starting out. So these first steps are a balancing act. Once you have established your lab with some core funding, you can start to be more imaginative and take greater risks.

**Why did you make the decision to move your lab to Dundee?**
It was a mixture of things. At Oxford I had a big teaching commitment, and though I enjoyed it, and the students were brilliant, I found it quite difficult to combine with a young family and a husband who, as a marine biologist, was at sea quite a lot. And then Cheryll Tickle had moved to Dundee, and there was a great nexus of developmental biologists there including others working on chicks, including Andrea Munsterberg and Kees Weijer. Everyone was working on different aspects of early development but there was a lot of technical and intellectual overlaps and many opportunities for collaboration.

The other thing that helped make this decision was that for my husband’s profession, living in land-locked Oxford wasn’t exactly ideal. He had done his PhD in the Sea Mammal Research Unit based in Cambridge, and they had recently moved to St. Andrews, which is only about thirty minutes from Dundee. Jonathan was offered an affiliation there and it solved our two body problem.

When I joined the School of Life Sciences at the University of Dundee it was a Wellcome Trust Centre and they’d just built a massive new building. We had funding for core facilities and this was all unlike Oxford, where departments were physically separated from one another and people had small areas filled with their own equipment. When I first moved up to Dundee, I brought with me one of my microscopes and set it all up, and when I came back in the morning there was someone sitting at it that I’d never met! The philosophy was completely different – you could go into any space and just ask if you could try this or that out, and ask for training. And with everything being in one building and all our lab spaces being shared, it was a very positive environment, and continues to be very positive. Just as an example, my lab is on the same floor as the MRC Protein Phosphorylation and Ubiquitination Unit, and interactions between this cohort of fantastic biochemists and developmental biologists is excellent and creates quite a unique scientific environment.

**In recent years your lab has done lots of live imaging of neurogenesis: what do these movies bring to the table?**
These days, the lab makes a lot of movies of cells as they undergo neurogenesis. While we set out to investigate a particular aspect of neuroepithelial cell behaviour – division orientation or neuronal delamination for example – because we are making movies we see all sorts of unanticipated things too. No one would fund you if you said you were going to film some cells and see if they do anything interesting, and yet observational science is a big part of what we’re doing, and out of it have come some remarkable findings, such as apical abscission – the regulated loss of the apical end of new-born neurons. Movies are great for that – you can play them back again and again, and each time you’ll notice something new.

**Where do you see chickens as a developmental biology model system in 2019?**
Well, like all models they’re good for some things and less good for others. They’re certainly much more robust for live imaging than...
mice embryos. Chicken eggs/embryos are used to the mother hen wandering off and cope well with changes in temperature: you can warm them up again and the embryos readily re-start development. If you try to do the same sorts of tissue manipulations we do in chickens in mice, the embryo is much less resilient.

Then there’s the question of how good a model it might be for human development – an area of research which developmental biologists are beginning to address. The early stages of chicken development are much more similar to human embryonic development than the mouse. Human tissue is rare and precious, and if you make important observations there, you will want to go to a model organism to pursue your question, and then come back with a very honed question to assess in human tissue. In that sense, you will always need model organisms. And we’ve learned so much from them, from the fly through to the mouse, and we continue to do so. It will be interesting to understand what aspects of development are human-specific, but we will only know that by comparison with model organisms.

More broadly, developmental biology is currently an exciting field. Which big questions will dominate the next decade or two?

Single cell ‘omics’ approaches are going to be very informative across developmental biology. At the moment I think that we’re in a bit of a surveying mode: it will be even more interesting when such analysis is applied to experimental contexts. It will also be interesting to map changes in tissues using spatial transcriptomics approaches – comparing transcriptomes within intact tissue (without dissociating and stressing cells) will be very important for understanding mechanisms regulating adoption and maintenance of cell fates.

The other area I’m becoming increasingly interested in is the developmental origins of human health and disease (the so-called ‘DOHaD’ field), and this has been stimulated by our recent work on the expression, function and regulation of an amino acid transporter. All sorts of metabolic genes that you would think would be fundamental to all cells are actually expressed differently in distinct cell populations in the embryo, and their expression alters in response to stressors. There’s a patterned orchestration of cell metabolism in the developing embryo which is just fascinating. There’s also the question of how gene and environmental interactions work, obviously a crucial part of DOHaD. You could be heterozygous for a mutation in a particular metabolism or signalling gene and this could have minor consequences until the embryo experiences a cell stress. For example, Sally Dunwoodie (Victor Chang Cardiac Research Institute, Australia) has done some very nice work on the effects of hypoxia on Notch pathway mutants and on FGFR signalling that I think is really insightful. We know so much about the signalling pathways that regulate development, and a key question now is how they are perturbed by changes in the embryonic environment. It’s an area of real fascination that is obviously linked to understanding how developmental defects arise.

Do you have any advice for someone considering a career in developmental biology?

One of the big challenges now is how broad a skill set you need to have. A postdoc in my lab has taught herself R so that she can write her own programmes and integrate data sets for single cell transcriptomics analysis: she wants to go on and be a PI, and knows she needs those skills to be at the cutting edge of developmental biology. It certainly helps to be interdisciplinary. So I would advise people to take advantage of a broad training as a PhD student, and be open to learning radically different skill sets. With new skills you are able to ask different questions. You can always collaborate with other people of course, but new skills shape your thinking too. I would also add that embryology is at the core of developmental biology – the task is to harness these new technologies to uncover developmental mechanisms.

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I understand you have a couple of family links to the arts?

My father, David Storey, was a playwright and novelist who started out as an artist. He was one of the so-called ‘angry young men’ of the 1960s, the generation of writers from the North of England, some of whom put on plays at the Royal Court theatre. His seminal work This Sporting Life was made into a film in 1963 by Lindsay Anderson. He continued as a novelist and playwright and won the Booker Prize in 1976 for his book Saville, which was about growing up in the north. So I grew up sitting in the stalls, sitting through rehearsals, watching plays based on my father’s formative years.

And my sister Helen is a fashion designer who used to design for Madonna and others. In the mid-1990s, the Wellcome Trust decided to start funding science art projects, and Helen and I thought why don’t we design dresses based on embryonic forms? Let’s combine what we’re both good at! And we did, and Wellcome loved it and funded it. The project was called Primitive Streak (http://www.primitive-streak.org/) and some of the pieces are still out there – the Neurulation dress is in the Reading Room of the Wellcome Collection in London, and the Lung Dress is in the National Museum of Scotland in Edinburgh. We’ve taken the exhibition all over the world and the designs attract a lot of interest and curiosity which opens conversations about science. One design for instance is a round, jewelled cage that a woman wears, representing an egg with various sperm hanging off it. But only one of the sperm is inside the egg: suddenly there’s a conversation to be had about how fertilisation works.

Is there anything Development readers would be surprised to find out about you?

There are some strange things I’ve done but they don’t necessarily tell you much about me – for instance I’ve swum with sperm whales in the middle of the Atlantic (an opportunity that came helping with my husband’s research). I swam away from the boat in the middle of the ocean and met a sperm whale eye to eye.