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INTERVIEW

Transitions in development – an interview with Margot Kossmann Williams

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Margot Kossmann Williams is an Assistant Professor at Baylor College of Medicine in Texas, USA. Margot uses zebrafish genetics, live imaging and embryonic explants to investigate how cell movements, such as those underlying axis elongation, are coordinated. We met Margot over Teams for a chat about careers, mentors and starting a new group just before a pandemic.

Let's start at the beginning: when did you first become interested in science?

I think my story is probably the same as a lot of people, which is that kids are naturally inclined towards science. I remember as a kid loving dinosaurs, bugs and animals. I went through a phase of wanting to be a paleontologist, because I was eight when Jurassic Park came out, and I went through a phase where I wanted to be a marine biologist. Science seemed like it would be neat to do, but I was too young to really understand what that meant. It wasn't until I was in college that it occurred to me that science could be a real job.

What happened in college that inspired you to become a scientist?

It was actually a particular person. I started at Muskingum College, a small liberal arts school in rural eastern Ohio, as a general biology major. I wanted to go somewhere that was far enough away from home (in central Ohio) that I could get some independence from my family – but not too far away. I wasn't exactly sure what I wanted to be, and certainly didn't think that I would ever go on to do a PhD. It ended up being really great for me. Because it was a small school, I was often one of maybe eight students in my classes. It meant I had lots of personalised attention from the professors, but I was also in this cohort with the same eight students, which gave us an opportunity to talk through different science problems and work through our labs together in a way that I don't think people can do if they're in a lecture hall with 300 other students. I had a professor, who during my second year, pulled me aside after a few cell biology classes and said, 'I don't know if you know this, but you're good at this and research is something that you should consider'. This one person planted that seed in my head.

Why did you decide to do a PhD and what attracted you to Ann Sutherland's group at the University of Virginia School of Medicine, USA?

Once that seed was planted, it just grew. I decided that a career in research sounded appealing, although I had no idea what it meant. Although Muskingum was great, it was hard when I was applying to graduate school, because there weren't a lot of active labs in which to gain research experience. The professors there are wonderful, and they do their research to the extent that they can, but it's a small school; they don't have the same resources as big schools. When I interviewed for grad school, it was a wake-up call. I realised that the other interviewees had been doing research projects in these big R1 universities for years. So, I did feel a little bit disadvantaged, but I want to be clear that there are a lot of people who run their own labs and went to small liberal arts schools – you can have the best of both worlds. There are definitely ways to still get the small school experience, but also get the research experience that one needs to get into grad school, such as making an effort to participate in summer research programs.

I was a neuroscience major in undergrad and when I went to the University of Virginia I rotated in two neuroscience labs. I had met with Ann Sutherland while I was interviewing and I fell in love with her because she's a warm, wonderful and kind person. She's also passionate about the work that she does, which is developmental biology; she works on gastrulation, pre-gastrulation and neurulation stage mouse embryos. Although I had never taken a developmental biology class in my life, I was drawn to her as a person and I decided to rotate in her lab. Then, sure enough, that's where I ended up.

What were your PhD projects?

First, I used live imaging to characterise primitive streak formation in mouse embryos at the onset of gastrulation. It was great because

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Development (2022) 149, dev200424. doi:10.1242/dev.200424

I overlapped with a more senior graduate student, Wei Wei Yen, who was co-mentored by both Ann Sutherland and Ray Keller. Through this collaboration, they became interested in murine gastrulation cell movements and had developed wonderful techniques to study them within live mouse embryos on a confocal microscope. While Wei Wei was studying convergence and extension movements during gastrulation, I started looking slightly earlier at primitive streak formation, using those same culturing and live-imaging techniques (Williams et al., 2012). Once those projects were done, Wei Wei and I both worked on another project characterising mouse neural plate morphogenesis, which I finished up after she graduated (Williams et al., 2014).

Your first paper was published in Development. How was that experience?

I was a second year graduate student when that paper was published (Yen et al., 2009). Wei Wei was the first author, but I contributed a figure or two to that paper, and helped with the revisions. When they first submitted the paper, I was pretty clueless because I was very new. I got a real taste of what the publishing process was like during the revisions; all of a sudden it was all hands on deck. I remember it being frantic, but fun and exciting. I think it was a positive experience and a crash course in the publishing process.

For your postdoc, you joined Lilianna Solnica-Krezel's group at Washington University School of Medicine, USA. What did you work on during that time?

There's been so much beautiful work done to characterise morphogenetic cell movements, thanks to the many live imaging techniques available. It is amazing to me that individual cell behaviours can shape the whole embryo, but how do they coordinate those movements? I knew I wanted to stay in development and I really wanted to learn more about the coordination of these morphogenetic cell movements in both space and time. As soon as I met Lila, I knew I needed to work with her. Lila's group does a lot of live imaging in zebrafish, which I was really excited to learn; zebrafish and confocal microscopy are just a match made in heaven. The project that I joined the lab to work on actually didn't pan out because the mutant didn't have the phenotype that we were expecting, which I think happens to a lot of people. When that didn't work out, I was a little bit deflated. I was struggling to know what to do next. Then, I took on a project on the *ugly duckling* mutant, which has disrupted convergence and extension during gastrulation. A former postdoc had done a lot of work characterising this mutant, but then ended up leaving the lab, so I came in to wrap up the project. It ended up being a very different story than we expected, which was neat (Williams et al., 2018). Meanwhile, I was able to start percolating the project that I wanted to take with me. My hope at that point was to go and start my own lab and that's when I transitioned into my second project. I started looking at Nodal signalling, using the *one-eyed pinhead* mutant, because Nodal is required for both embryonic patterning and morphogenetic movements. My question was: how is patterning along the anterior-posterior axis translated into extension along that same axis?

During that time, you received a NIH Pathway to Independence Fellowship (K99). How did that come about?

The K99 is almost a mythical entity; when we all start our postdocs, it's like 'maybe one day I can get a K99!' It wasn't until I started working on my second postdoctoral project that I realised I might actually have a chance. The biggest thing is finding a project, not just the project that you're working on in the lab, but something that you can really envision for the future of your career. I knew that it wasn't going to be funded the first time around, but I wrote it up anyway because I wanted to get feedback. I would advise people to figure out when your last cycle of eligibility is (based on when you got your PhD) and then calculate back from that, so that you have time to submit twice. Just as I suspected, my application was not funded the first time around – it shouldn't have been – but I was able to get feedback from reviewers that really helped me strengthen it. So, when I turned it around for a resubmission it actually was funded, which was wonderful.

At what point did you start looking for independent positions?

I started looking in the fall of 2018. I tried to make sure that I had my application package pretty much put together before most of the jobs came online, so that I could apply to them when the deadlines came. Applying to get a new job is a full-time job! I cast a very wide net. I ended up applying for almost 50 jobs, which is not uncommon. I applied to essentially any position that had 'biology' in the name, particularly developmental biology, but there aren't a lot of developmental biology departments around anymore. It's a lot of effort – and it's worth it – but be aware it takes time.

Why did you choose to accept a position at Baylor College of Medicine?

I think the biggest choice for me, and I suspect for many people, was deciding between a medical school and a school of arts and sciences. There are definitely upsides, as well as downsides, to both. I had always assumed that I would end up in a school of arts and sciences, because my work is fundamental and I love teaching. But when I received this offer from Baylor, it ended up being my future colleagues and the resources available that sold it. For example, we have a lot of other biomedical research institutes close by and lots of core facilities.

The approach that I took was to hire the people for themselves, and not for the skill set. You can teach a person skills, but you can't teach somebody to have a good attitude!

How was it setting up your lab in 2019?

It was equal parts fantastic and terrifying. It was wonderful because it's surreal and fun to say, 'wow, this is my lab and I get to decide what the priorities are, what the first experiments are'. Bringing people in for the first time was also really wonderful. I had a graduate student who joined right away, followed by a technician and then a postdoc. To start passing along the skills, and more importantly the passion, was really fun, particularly because developmental biology is not something that people usually have a strong foundation in. To be around somebody who's never really thought about how amazing embryos are and then, over the course of an 8 week rotation, to see them come around and say, 'oh my gosh, embryos are amazing!' – that was really fun.

There were some challenging parts, of course, and it was not made easier by the pandemic because everything shut down about 4 months after I started my lab. I imagine that a lot of people at all stages of their career were negatively impacted by the pandemic. It was pretty disruptive to have our research completely shut down, but

Development (2022) 149, dev200424. doi:10.1242/dev.200424

at least I got in, got my freezers ordered and stocked up on pipette tips before the current global shortage of these things. The hardest thing was trying to keep a brand new group together, to have it feel like a lab unit. We met a lot virtually – and maybe my group thought it was annoying that we would check in every day – but I just wanted to anchor people and let them know that they had a lab home. One of the most challenging parts for me was making the transition from being bench focused as a postdoc to suddenly wearing a lot of different hats. The administrative stuff, the teaching stuff, the training, the hiring – all of these things were not part of my formal training before. It can be a bit overwhelming but, ultimately, it's been fun.

What approach do you have for hiring new people?

The approach that I took was to hire the people for themselves, and not for the skill set. You can teach a person skills, but you can't teach somebody to have a good attitude! I think if you can find somebody who is excited and passionate, bring them in because that's the kind of energy you want in the lab, then you can teach them to do whatever it is they need to do.

What are your views on mentorship?

I have strong opinions about mentorship. For those of us who didn't have scientists in our family, and didn't really know how to navigate the academic environment, having people who are willing not only to provide advice to us, but also to advocate for us, is so important. A great mentor is not just somebody who tells you what you should do. It's somebody who actually puts their time and effort into contributing to their mentee's success. I've been incredibly lucky to have multiple different mentors throughout my career, who have both provided great advice, but also really advocated for me in a way that I think I probably wouldn't have succeeded if it weren't for their help. I really want to be a good mentor to my trainees, because I benefited enormously from this wonderful mentorship and I really want to pay it forward.

Do these views contribute to your lab philosophy?

It's all about keeping things in perspective. I don't think that my biggest influence will be via the science itself; I expect that my biggest influence will be on people. If I can train people to do rigorous research and design experiments well but, more importantly, to love science, I will have done my job. Regardless of what trainees in my lab are working on, it's more satisfying to know that they came out of grad school feeling positive about academia and science. So, that leads to the lab philosophy that people have to come first. Yes, our science is important and, yes, we'll do the best science we can, but the training and education that people receive is the most important thing.

One of the best pieces of advice I can give is that you don't have to do it alone

Do you have any tips for people starting their own group?

One of the best pieces of advice I can give is that you don't have to do it alone. If you have a good network of people from your postdoc or even within the structure of your new position, those people are generally willing to help you, if you reach out to them. I had several colleagues during my postdoc who were both formal and informal mentors to me, and I relied on them a lot. One of the other things that made the transition easier was having really great administrative folks in Baylor. I can't stress enough: when looking for jobs, look for a place with a really strong administrative structure. These people are amazing; they know the ins and outs of these institutions in a way that I never will. Something else to remember is that there's more than one right way to succeed in science. As you embark on your job-search journey, you're going to get a lot of advice from people. Almost all of it is good and well intentioned, but that doesn't necessarily mean that it's right for each of us. It actually caused me a lot of anxiety to try to follow everyone's advice exactly. I felt better when I was able to let go of that stress and do things in my own way.

What are the research themes in your group at the moment?

I'm interested in the coordination of embryonic cell movements in both space and time, which we are studying in the context of embryonic axis extension during gastrulation. We are using zebrafish embryos, as well as this cool zebrafish embryo explant system, which is something that I started during my postdoc based on techniques that were developed in the lab of Christine and Bernard Thisse (Xu et al., 2014), and Hazel Sive before that (Sagerström et al., 1996). We isolate the animal-most cells of the blastoderm, and then we can give them different signals to see how they respond. It's an excellent system to test for molecules that are not only necessary but also sufficient for some of these embryonic cell behaviours. We are also following up on Nodal signalling, specifically its role in morphogenetic cell movements independently of its better understood roles in tissue specification. We have a list of candidates that we're working with now to identify the molecules that function downstream of Nodal signalling and bridge that gap between patterning and morphogenesis, which we term 'molecular translators'. Finally, since I joined Baylor, we also have a couple of new collaborations in which to apply this fundamental knowledge about morphogenesis to neural tube closure defects. These collaborations are great and they're taking us in new and interesting directions.

How did you carve your research niche?

When I started in grad school, I read all these papers about morphogenetic cell movements. There has been some absolutely fantastic and mind blowing work done over the past several decades, figuring out exactly what these cells are doing. But I always wanted to know a little bit more. There was this gap: the cells are executing these complex behaviours, and it's incredible, but how do they all know to coordinate together to make an embryo? It's such a huge question and I know I'm not going to come in and solve this by myself but, if I could take a small bite out of it, I would be happy. I hope the niche that we've made is to take some of these well-known factors (like Nodal), but try to think in a slightly different way about what their roles in morphogenesis might be.

What excites you in your field at the moment?

I am in awe of all the work that's been done recently in the field of synthetic morphogenesis. Not only can people make all of these different embryonic cell types in a dish, but they're now able to make tissue-appropriate structures and undergo tissue-appropriate morphogenesis. I think that's absolutely remarkable.

Have you ever considered a non-academic career path?

For a long time, I strongly considered teaching at a smaller school, similar to the college that I went to. The biggest reason for that was because, like I said, I attribute my entire entrance into the academic world to this one professor who recognised an aptitude in me and was kind enough to say something. The idea of being that person – even just for one other student – is so appealing to me.

Development (2022) 149, dev200424. doi:10.1242/dev.200424

Finally, what would Development readers be surprised to learn about you?

Well, most people are surprised when I tell them I'm an identical twin!

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