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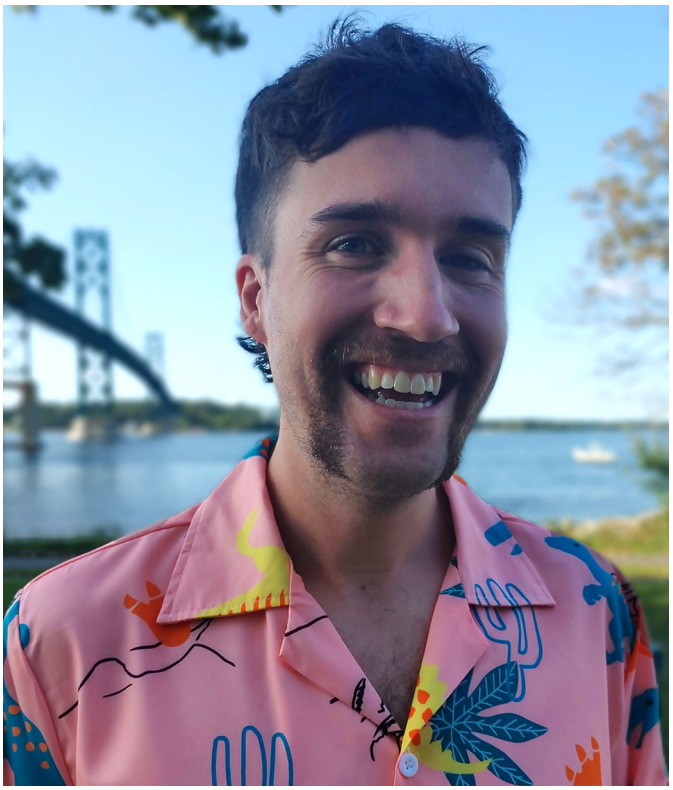
INTERVIEW

An interview with Tyler Huycke

Daniel Routledge*,‡

Tyler Huycke is a postdoctoral researcher in Zev Gartner's and Ophir Klein's labs at the University of California San Francisco (UCSF), where he studies the relationship between mechanics and tissue patterning during gut morphogenesis. Tyler served as an editor for the Journal of Emerging Investigators and as a student co-leader of the developmental and regenerative biology graduate programme at Harvard University. He was awarded the Young Investigator's Award at the 2022 Santa Cruz Developmental Biology (SCDB) meeting, which celebrates outstanding early career researchers. I caught up with Tyler at the SCDB meeting to discuss the award, his research and his career.



First of all, congratulations on winning the young investigators award here at SCDB. What does it mean to you to win this award?

Well, it's really a huge honour. I was shocked when I first heard the news, but it means a lot to me because I've been a developmental biologist since I started my career in research. So, to receive an award from the community that I'm really passionate about, and one that I see myself being invested in throughout the rest of my career, means a lot to me. It's also been great to be here at the meeting, to connect with former friends, meet new people and share my research with everybody.

Rewinding back to the beginning of your career, when and how did you first become interested in science?

This is kind of interesting. I tried to pinpoint it and I realised I don't really have an 'a-hah!' moment where I realised that science was for me. It was actually more figuring out what I don't like, and seeing what was left, which was biological sciences in general. When I started as an undergraduate at the University of Oregon, probably like many students, I sat in my introduction to chemistry course and the teacher asked all the students to raise their hands if they were pre-medicine, and around 95% of the class raised their hand because everybody had to go through chemistry. And the teacher said, 'there'll only be two of you at the end of this'. And then, sure enough, I eventually realised that I was more into the science behind the medicine as opposed to the application of it. I also realised I was more of a biology person – I just got more excited by taking pretty images and running gels and things like that, as opposed to running reactions in a flask. So, that was the beginning of what got me interested in biology; figuring out I didn't like the other things seemed to work.

Then how did you become interested in developmental biology specifically?

My interest in developmental biology was actually also by chance. I didn't know what developmental biology really was until I took a course in it as a junior during my undergraduate training, and I actually hated it. I didn't like the course I took at all. Then, a couple of months later, I was at a science event at the time, where labs were trying to get undergraduate researchers to come to work. There I met Jared Talbot and April DeLaurier – Jared was a graduate student and April was a postdoc in Chuck Kimmel's lab at the University of Oregon. They got me really interested in fish skulls and I thought, 'okay, cool'. I was interested in getting some lab research opportunities and they said 'yeah, come on up to the lab'. Then I think I started in the lab the next day, and then just fell in love pretty much instantly once I was working with zebrafish and started doing live imaging, just watching development happen. I think that was what I was missing in the course that I hated; it was just very 'textbook' and I didn't get to see the connection between cartoon schematics and this amazing biology happening in 4D. I really feel like seeing is believing, because when I saw the zebrafish embryo elongate, grow its somites, break out of its chorion and start swimming around, it was just too cool. I had to figure out how it worked. I guess this relates to a larger discussion that we've

*Reviews Editor, Development

‡Author for correspondence (daniel.routledge@biologists.com)

D.R., 0000-0001-8328-5061

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had actually at this meeting of how to re-ignite excitement in developmental biology. I think this will be really important moving forward – we really need to figure out a way to get the younger generation excited and make the connection that pretty much everything is developmental biology; cell biology, biochemistry, genetics…developmental biology is the manifestation of it all. So, I was lucky to just stumble into the Kimmel lab by chance and that just kick-started everything for me.

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You impressively achieved a first author paper out of your undergraduate work at the University of Oregon, quite fittingly published in Development. Can you tell us a bit about that project and how that came about?

Pretty much that day when I went to meet Chuck to see if I'd be a good fit for doing undergraduate research in his lab, he connected me with a postdoc in the lab, Brian Eames (who now has his own lab at the University of Saskatchewan). Brian was very helpful in getting me started on a project that was looking at whether Indian hedgehog (Ihh) mutant zebrafish had similar phenotypes to the *Ihh* mutant mice that had been described. It turned out that the fish didn't have the same phenotype, probably because there is an IhhA and also an IhhB so there's probably some redundancy. But as I was sorting through embryos, I started noticing that the ones with a genotype positive for the mutants actually had a bone phenotype, which we weren't looking for at the time. I figured out that this phenotype was really consistent across all my mutants with 100% penetrance. I decided that I would turn that into a project and asked, 'how do dermal bones get their shape?'. It was a really fun project from start to finish that started out with just a random observation. I'm very grateful to Brian and Chuck for giving me the freedom to just go with it. I stayed on in the lab as a technician after I graduated to see the project to completion; at that point, I'd decided I wasn't going to medical school and I still had a lot of friends in Eugene so it was a really good opportunity I couldn't miss.

You then moved on to Harvard for your PhD, where you studied morphogenesis of the smooth muscle layers in the gut. Why did you choose to work with Cliff Tabin and what were the questions that you set out to address?

Coming from Chuck's lab, I was really enamoured by zebrafish as a model organism, so the first two labs I rotated in were zebrafish labs. Everybody then said, 'do something else for your third rotation'. I thought 'well, okay, I'll do something else, but it's still going to be developmental biology'. And Cliff Tabin's lab seemed like a great place to be – I'd heard nothing but awesome things about it. So, I ended up in Cliff's lab and started working on the chick embryo. I had never touched a chick embryo before. I remember the first time I cracked open an egg to do a gut dissection and there was this feeling of 'whoa, this is totally incredible'; a completely different scale compared to working with zebrafish. That's when I realised that there is a whole different set of tools for the chick, and that we could use this embryo for looking at things that the zebrafish was less ideal for. Amy Shyer, who was finishing as a graduate student at that time, taught me all the ins and outs of chick gut morphogenesis. Then things just developed from there. I was really excited about the work in the lab and the diversity of the different types of projects being carried out, ranging from development to evolution. It was a zoo of a lab; we had emu eggs, quail eggs, snails and seahorses…the list goes on. So, I think I was just interested by the cool, weird science and the possibilities in the lab no matter what avenue I pursued. I eventually settled on studying how the muscle layers of the gut become organised during development, and this project led me to my current research interests at the intersection of tissue patterning and mechanics.

While you were at Harvard, you were a student co-leader of the developmental and regenerative biology program. What did this entail and what aspects of this role did you enjoy the most?

This is relevant to another theme that came up in our discussions here at this conference, that quite often developmental biology doesn't have its own department. This was somewhat true at Harvard, where the developmental biology labs were spread throughout the different departments: genetics, cell biology, biochemistry, and so on. Not only that, but they were also across different campuses. The goal of the developmental and regenerative biology programme was to bridge all of those campuses together and generate a community not only for the students, but also for the faculty, because we all lived and worked there in close proximity, yet sometimes we wouldn't see each other for months. So, it created a great community for networking across all the different levels of training with the faculty and it really was a community-building effort. We had a seminar series and an annual retreat, and then we did a field trip to the Northeast Regional society for developmental biology meeting. I think they still go every year.

What led you to then join Zev Gartner's lab at UCSF to look at the interactions between mechanics and tissue patterning?

I had interviewed with several labs for postdoctoral positions, but I was attracted to Zev's lab because of a paper I had seen on how mesenchymal compaction can drive tissue morphogenesis. I emailed Zev out of the blue and came out here to San Francisco for an interview. Again, I was really drawn to the diversity, as in Cliff's lab; you could pick whatever question you wanted to do and run with it. And then with Zev's lab, it was a lot of different model systems and people from a lot of different backgrounds; they had computational biologists, systems biologists and cell biologists, but there wasn't really a developmental biologist in the group. And so I brought my own unique perspective, whilst benefitting from the multidisciplinarity provided by everybody else; I was continuing to do developmental biology, just through a slightly different lens than before. My project naturally evolved into a collaboration with Ophir Klein's lab. Each lab provides non-overlapping areas of expertise and resources – Zev's lab with tissue engineering and cell biology and Ophir's lab with stem cells and development – so I work at the interface between these two interdisciplinary groups and I greatly value the collaborations that are enabled by this.

At the talk you gave here at SCDB, you showed some data from multiple model organisms; you had chick, mouse, organoids…and I know you've previously worked with zebrafish. What would you say are the benefits of having worked with so many model organisms already?

There are so many benefits to working with multiple model organisms. For one, when you go to a conference like this, you can relate to a lot of the different talks and posters, and pick up on little nuances of the different systems. Then, from a more practical

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standpoint, you can figure out which model organism is good for different questions you might have. For example, the genetic toolkits for some model systems might be better, but the manipulation might be easier in others, e.g. mechanical or physical perturbations. For these, you need to have larger tissues that are a lot easier to work with. So, it's fun to see the breadth of tools available and then also, in an evolutionary sense, how these different organisms figure out how to deal with the same problems. Sometimes these are achieved in different ways, like the folding patterns of the tissue or the time it takes an organism to develop. I think the comparative approach is really powerful to learn more about the underlying biology and no single model system is the best.

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Which model organism would you say is your favourite?

My favourite is probably always what I'm currently working on and so right now my favourite is the chick, which is easiest to work with. I love the fact that I can just order chicken eggs to my lab door, put them in an incubator for a couple days and then take them out to get exactly the right stage. I don't need to go to the mouse or zebrafish facility, and therefore save much time!

Looking ahead, I understand you're planning to apply for tenure track faculty positions. In which direction would you like to take your future research?

There are so many directions to take the research, it's often hard to pinpoint exactly where I want to go next. For the current work that I'm pursuing with Zev Gartner, we can either go upstream or downstream of the problem to figure out what the signals and forces catalysing these morphogenetic events are, but also the downstream consequences on not only morphology, but overall organ function and regeneration. I'm really interested in also applying some of these core principles that we're learning about tissue folding in the gut and seeing if those same principles are utilised in other contexts or systems to generate either similar or different morphologies. I'm currently brainstorming potential avenues to go down and I haven't committed to anything yet, but stay tuned.

And finally, is there anything our Development readers would be surprised to learn about you?

I guess one thing is that I produce electronic music, so keep an eye out for my new album later this year once the paper comes out, and we'll put the link up on SoundCloud.