

INTERVIEW

Pathway to Independence – an interview with Yuchuan Miao

Yuchuan Miao is a Postdoctoral Researcher at Harvard University, USA, where his research focuses on the development of *in vitro* stem cell models of somitogenesis. Yuchuan has been selected for Development's Pathway to Independence Programme and we caught up with him over Zoom to find out more about his research background, his hopes for the programme and his future research questions.

Starting at the very beginning, how did you first become interested in science?

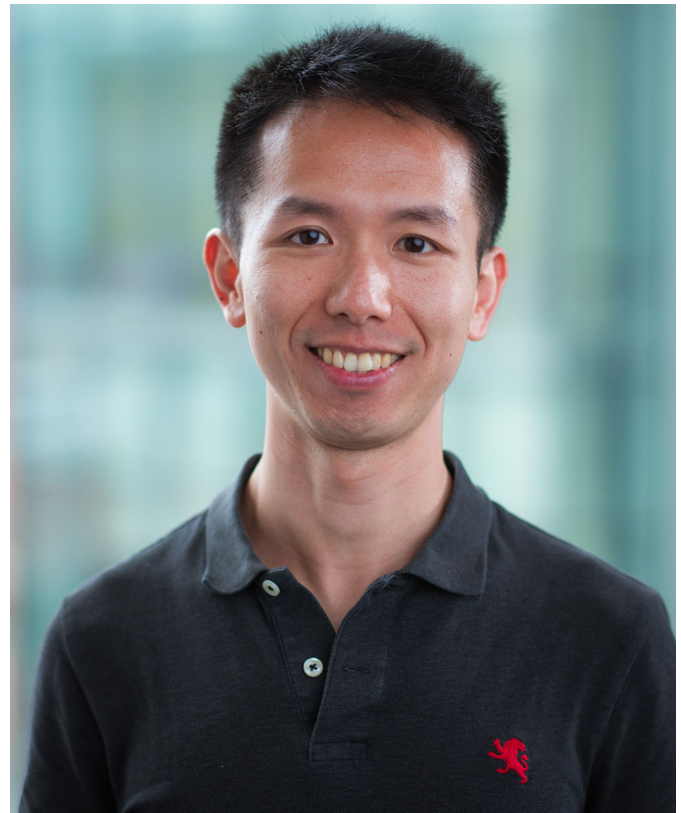
I think it was early contact with nature; during my childhood, I grew up around woods and mountains, and I spent a lot of time playing in the woods after school. Even as a child, I really appreciated how beautiful nature is; I would collect leaves, flowers and insects of different colours. Then as I got older, I became more curious about how these things work and how nature makes these beautiful patterns and shapes. Also, my dad was always interested in science, but never had the chance to pursue it. So I remember he would always find me books about science or nature whenever he came back from work, and I think those books also inspired me to pursue a career in science.

You completed your PhD in 2019 at Johns Hopkins University, MD, USA, where your research focused on cell migration. What questions were you specifically trying to address?

Working with *Dictyostelium*, a single-cell amoeba, I was focusing on what determines different modes of cell migration, as cells can migrate in a number of varied ways; for example, some cells move like amoeba, while others, like fish keratinocytes, can 'glide' like a fan. So I was interested in the question of 'what makes the cells move differently?'. I found that these different migration mechanisms are controlled by spontaneous signaling and actin waves found in the cell cortex. I developed several techniques to perturb these waves to make them go faster or slower, and found that each perturbation made the cells switch their modes of migration. Eventually, I found this causal link that cortical actin waves control the type of protrusion that cells make, which in turn controls the cell migratory modes. I think that one implication of my work is that we used to view cell migration mostly as being idiosyncratically controlled by different proteins, but my work suggests that these different modes exist in a continuum and are not so different from each other.

You then moved to Harvard University to join Olivier Pourqui's lab for your current postdoc, where you have switched fields to work on *in vitro* models of somitogenesis. What prompted this switch and why did you decide to join Olivier's lab?

Because I was working on wave patterns at the single-cell level, this really got me interested in pattern formation in general. Then, when I was looking for a postdoc, I discovered that there's really no better place to study pattern formation than in developmental



biology. As I then learned more about development, I came across some movies about somitogenesis, which were so amazing to me because these films showed how, one by one, somites formed and how this was precisely controlled by the segmentation clock. At that time, I also wanted to use a cell-based model to study development because I am a cell biologist by training, and I wanted to see how cells orchestrate development in real time, which is much harder to do in real embryos. Then I came across Olivier's lab, which has been focusing on somitogenesis for decades and developing stem cell models to recreate these early somitogenesis events. Therefore, I contacted him, he invited me for an interview and I gradually learned that there is a great environment in his lab, people are very happy and he's a very nice person, so I decided to join his lab working on somitogenesis using stem cells. Although appearing to be quite different topics (between my PhD and postdoc), the common theme is waves and pattern formation.

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Could you tell us a little bit about the somitoid and segmentoid models you have developed? What are the most challenging and exciting aspects of working with these models?

In development, somites form sequentially from the anterior to the posterior in coordination with the elongation of the body axis. It's a

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very complicated process, and the first model I developed, the somitoid, is a simplified model. Instead of sequential formation and maturation, the cells in this model differentiate and form somites at the same time. Even though the somitoid does not capture every feature of somitogenesis, it is much more experimentally friendly and much easier for characterization and perturbation. For example, this model is attached on a flat surface, so it's much easier for higher resolution imaging. On the other hand, the second model, the segmentoid, is designed to recapture the spatial and temporal features of somitogenesis, and to model the sequential formation of somites, including the oscillating signals and gene expression dynamics involved in patterning this process. Experimentally, the segmentoid is a little harder to work with and image, as it is embedded in Matrigel, but it can serve as a proxy to test certain insights we cannot in the somitoid model. Overall, the back-and-forth use of these two models is a really great tool for dissecting mechanisms of pattern formation in somitogenesis.

How did you hear about Development's Pathway to Independence Programme and why did you decide to apply?

I first heard about it on Twitter, and I think it's a great initiative, as I think we need more programmes or initiatives to help postdocs to transition into independent positions. To me, the programme represents great recognition by the community. It pairs a postdoctoral fellow with an established scientist for close mentoring, which is a precious opportunity very few programmes provide. So, there is simply no reason not to apply.

What do you hope to get out of out of the programme?

I would like to increase my visibility and profile in the community, and I hope to get some training on skills that we don't get during postdocs or at graduate school; for example, how to do interviews, how to start a lab, how to do chalk talks and things like this. I think that would be really complementary to the training of our academic institutions. Also, I hope to establish connections and friendships with other fellows in the programme, as we are all at similar career stages. I hope we can form a bond to share experiences and give each other support in our future academic careers.

Where are you in the process of securing an independent position and what has your experience been so far?

I'm starting to apply this year; most of the deadlines are this Fall, so I'm currently in the process of preparing all the materials and thinking about applications. It's really an exciting time since I get to sit down and envision all the things I want to explore in the future. At the same time, it can be stressful because there is a lot of work to do to prepare for the applications on top of my research and other duties, including visa applications. Securing an independent position is very competitive and the uncertainty can be a bit overwhelming, but being part of this programme will help with some of that stress.

What excites you most about becoming an independent researcher?

I think it's a privilege to work at the frontline of research to expand our scientific knowledge. The feeling after every small or big discovery is pure happiness. Just like everyone else in my field, I will continue be amazed by what stem cells can do and I look forward to being one of the drivers of these discoveries. Outside the lab, I am also looking forward to the satisfaction of mentoring. I really enjoy closely mentoring students or postdocs; I think the satisfaction of mentoring is a special feeling associated with

academia, being able to help other people grow and develop their skills. I recently saw one of the students I mentored in graduate school had received a really great recognition award from the American Society of Cell Biology, which made me really happy.

And conversely, what do you think will be the most challenging aspect of being a PI and how will you prepare for it?

I think the most challenging part will be how to manage the many different aspects of being a PI, including managing budgets, hiring people, etc. These are things we have never done before, so naturally there is a little bit of stress around it. But there are a lot of workshops I have seen that I plan to attend the future; for example, a new PI training 'bootcamp'. I also like to shadow my lab manager to help prepare for the logistics of running a lab, to learn about how to order and buy things, stock reagents and generally keep on top of things. I hope these experiences will give me the best start possible.

How important has mentorship been so far in your career and how do you think you will approach being a mentor to others?

Good mentorship is extremely important to me, and I think I've been extremely lucky to have the mentorship I did during my PhD and postdoc. I love the kind of mentorship that gives you the freedom to explore and to let you think for yourself. For example, my PhD supervisor, Peter Devreotes, and I never had a lot of structured meetings; he would always just come into the lab, bring a coffee and sit down with me and say, 'so what's up? What's going on?'. Then we would chat for a while about any problems or what I'm thinking about my results. That kind of informal chatting really encourages you to think and to develop your independence, and that is the kind of mentorship I hope to offer to anyone who joins my lab in the future.

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Is there any place in particular where you would like to start your lab?

Although I would prefer big cities in general, I don't think there is a particular city I have focused on. I am already more familiar with the US system and most of my friends are there, so I would probably go with the east or west coast of the USA. However, I am also keeping my options open and looking at other countries, such as the UK and Switzerland; I also like the idea of learning and adapting to a new environment.

What research questions would you like to address with your own group?

In general, I am hoping to continue using stem cells to model human development, focusing on the cell biology aspect of pattern formation. More specifically, there are probably two directions I would like to take in parallel. First, I will continue using the system(s) I have built to study the mechanisms of somitogenesis, focusing on the cell biology aspects. The *in vitro* models are the perfect playground for me to identify interesting cellular behaviours and integrate them with what we already know, mostly from the angle of genetics. Second, I would like to eventually build a human body in a Petri dish. So far, I've been developing several models of somitogenesis and body axis development. In the future, I want to start generating models for the developing limbs, another important

part of our body plan. There are currently no sophisticated 3D stem cell limb models, so I hope to fill this gap and understand human limb development better, which could have really useful purposes in the future for regenerative medicine, for example. Given my training with Olivier and background in developing stem cell models, I think I'm the right person to do this.

Did you ever consider an alternative or non-academic career path? If so, what was it and why?

I did consider going into industry for a little bit, but I quickly decided that's not for me; I would want the freedom of choosing my research direction and also, as I mentioned earlier, the satisfaction of being able to mentor PhD students and postdocs. If I was to think outside science completely, I would say I might do

something in the film industry. I've always liked the idea of film-making, and I kind of think of myself as a film-maker, because I spend my time making movies of cells; I'm the director and my stem cells are the stars.

Finally, is there anything Development readers would be surprised to learn about you?

I used to be in an acapella group in graduate school (I sing tenor). I never actually got professional training, it was just for fun, and is something I will enjoy getting back into if I find the time!

Yuchuan Miao was interviewed by Daniel Routledge, Cross-title Reviews Editor at The Company of Biologists. This piece has been edited and condensed with approval from the interviewee.