

## INTERVIEW

## Pathway to Independence – an interview with Loic Fort

Loic Fort is a Postdoctoral Fellow in the lab of Ian Macara at Vanderbilt University. He is interested in understanding cell fate specification through the lens of mechanobiology, using 2D and 3D human stem cell systems. Loic is one of the first fellows in the new Pathway to Independence Programme – set up by Development to support postdocs as they navigate the job market. We met Loic at the recent Society for Developmental Biology Annual Meeting in Chicago to talk about his career so far and his plans for the future.

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

Weirdly, I think it was watching my parents cooking. Initially, I wanted to become a chef, and then I realised that, actually, science is very similar to cooking – it's just that you follow a protocol rather than a recipe. And then I really got on the science track when I got an internship at an early stage during my Bachelor's degree – working on a *C. elegans* model of muscular dystrophy. I then went on to do a Master's degree, and spent the second year of that in Montreal. I had realised by that time that science is international, and my English was terrible. Montreal seemed like a good option because it's a mix of French- and English-speaking, so I spent nine months at the Institute for Research in Immunology and Cancer, and then went back to France to graduate.

### You moved to the UK to do your PhD with Laura Machesky in Glasgow. Can you tell us a bit about why you chose to move there, and what you worked on?

During my Master's, I'd got really interested in the cytoskeleton, and in how cells move. I wanted to be in Europe, but was pretty flexible with location, and one of the PhD programmes I applied to was at the Cancer Research UK Beatson Institute in Glasgow. That's how I ended up in Laura's lab. When I started my PhD, a previous graduate student had done a big screen to identify new regulators of cell protrusions. One of the proteins they found was completely uncharacterised, and one part of my project was to characterise it. It was exciting, working on an unknown protein, but also frustrating – because there was no literature on it. We managed to figure out what it was doing, and the other cool thing about this project was that we got to name the protein (CYRI) – which is pretty neat as a student.

### After this, you moved to the USA to work with Ian Macara at Vanderbilt. What attracted you to his lab and what have you been working on during your postdoc?

I wanted to work with Ian to learn more about cell polarity. I ended up drifting towards working with human induced pluripotent stem cells (hiPSCs), because we realised that they are actually extremely epithelial, and we started asking questions around when cell polarity gets lost during differentiation. So what we've been doing is

differentiating hiPSCs to cardiomyocytes, and trying to figure out



some of the pathways that regulate cardiomyocyte differentiation. We found that a subpopulation of cells undergoes apoptosis during differentiation, and these dying cells release metabolites that will bind to receptors at the surface of the surviving cells and will license them to respond to the differentiation cues. We uncovered a non cell-autonomous pathway that drives cell differentiation through apoptotic release of metabolites. We don't yet know whether something similar happens *in vivo* during heart development, but we do know that there is a lot of cell death in the early embryo, and that's not really been investigated much yet. I find this really interesting – the idea that dying cells aren't 'useless' but that they can act as messengers and regulate the fate of neighbouring surviving cells.

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

In Autumn 2022, I went to a conference organised by Development and The Company of Biologists [the most recent in the journal's series of 'From Stem Cells to Human Development' meetings] and this is where I heard that the journal was planning to launch this programme. So I kept an eye on this, and saw the announcement of the call for applications. At that point (January 2023), I was starting to think about going on to an independent position, and I thought the programme could help me gain new knowledge and skills for how to become a PI.

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

I'm really hoping to meet new people that are in the same situation as me – there are plenty of people going through the process of applying for independent jobs, but you can feel quite alone. So I think that having this kind of community will be very useful –

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obviously there are channels like Future PI and New PI Slack, but I'm looking forward to meeting the other PI fellows face-to-face and sharing our thoughts. I'm also looking forward to gaining new skills that you don't get during PhD or postdoctoral training – like hiring and managing people, building a group and so on – these things seem pretty stressful!

### **I'm also looking forward to gaining new skills that you don't get during PhD or postdoctoral training**

#### **Where are you in the process of securing an independent position and what has your experience been so far? What are you looking for in deciding where you'd like to set up your lab?**

I'm only just starting – I've already put down some big ideas for my research statement, and I'm working on the other elements I'll need for an application, but I still have a lot of work to do before I start applying for positions – which I'm planning to do later this year. For me, the location is not that much of a deal. I have moved across four different countries for my training, and I feel pretty comfortable adapting to a new environment. The main decisive factor will be to find a department or institute that will be the right fit for my development as a scientist, where I could develop ideas. I also want to bring something new to this department. Finally, I really want to find good colleagues to work with.

#### **What excites you most about becoming an independent researcher?**

I think it's mainly the opportunity to investigate the questions that interest me the most. What really drives me is making discoveries and creating new knowledge – it doesn't happen all the time, but the possibility is what excites me. I am also very excited to mentor the new generation of scientists and create an environment where they will feel comfortable, regardless of their background. Giving an opportunity to do research to anyone truly interested by science can make a difference to that person, similar to what happened to me when I applied for this summer internship 15 years ago.

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

Funding, I guess! I think that's the part that I'm really not comfortable with – writing grants and being responsible for funding for other people is something that scares me a bit. I think I've gained good knowledge about how to write fellowships during my postdoc, but this will be a whole other level – not just focussing on the detail of the experiments you want to do, but really writing about the broad ideas and the impact they will have. I'm also a bit nervous about switching from spending most of my time at the bench to being in an office – even though I know as a junior PI, I will be expected to still spend time doing experiments, I think it's going to be a bit of a weird transition!

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

I really want to understand the connection between the physical world and the biological world – how forces can affect cell fate differentiation. This is what I've been working on during the second part of my postdoc and I've started generating preliminary data. To me, it's fascinating how the outside world can have such an influence on

gene expression. The mechanobiology field has become very trendy, but I still think we have a lot to learn. Whenever I see an embryo undergoing morphogenesis, and people are talking about the genes that regulate it, all I see are forces – compression, relaxation and so on. To start with, I expect I'll be using mainly stem cell systems, but in the long term I'd love to be able to test what we discover back in the embryo – either in my own lab or through collaborations.

### **I really want to understand the connection between the physical world and the biological world – how forces can affect cell fate differentiation**

What's exciting is that I can only start to think about these questions because of the technological advances in bioengineering and biophysics in recent years. I'm really interested in how you integrate different disciplines to answer a question. I think I got this early on from Robert Insall [at the Beatson Institute], who is a biologist but thinks a lot about the maths – it always fascinated me that someone can understand biology using equations.

#### **Thinking about the bigger picture, what are the most exciting advances and open questions in your field right now?**

The development of protocols to recapitulate early stages of mouse and human development (pioneered by the Zernicka-Goetz and Hanna labs) is probably one of the most exciting areas in developmental biology. With the proper ethical regulations in place, it will allow scientists to obtain new data about cell specification, tissue patterning and morphogenesis.

#### **How important do you think mentorship is in navigating an academic career?**

I've been extremely lucky to have very good mentors all the way through from my Bachelor's until now, as a postdoc. I think the biggest thing it's taught me is that you need to tailor your interactions with people based on their personalities. I'm more of an introvert compared to other people in the lab, and watching my mentors adapt their communication to get their message through to different types of people has been very instructive.

#### **I understand you're a first-generation college student. What challenges did this bring in starting out your academic career?**

It's interesting: I never really thought about this until I moved to the USA – in France, this wasn't really something that got talked about. But when I look back, there were definitely challenges in navigating the system – there were people to help me within the academic system, and I'm very grateful to them because for me, it actually went pretty smoothly. But I think that the fact I had to do things by myself is one of the reasons I've become interested in outreach activities.

#### **Can you tell us a bit about the outreach you've done and why you think it's important?**

I started getting involved at the Beatson Institute, where they had open door nights for underprivileged schools across the greater Glasgow area. I really enjoyed showing kids the kind of science we were doing and explaining why it's exciting. And what I realised was that the students, who were young teenagers, had exactly the same kind of questions that we had – of course they didn't ask them in scientific language, but they wanted to know the same things that

we were trying to figure out as cancer biologists. To me, this really showed that everyone can think about science even if they don't realise that's what they're doing.

At Vanderbilt, we've been trying to implement something similar. There's a great outreach committee and they've been starting to do events where school kids can rotate through different labs for half a day and see what people are doing. In the lab, I've been mentoring high school and undergrad students – just trying to show them how fascinating developmental biology can be. Not many people have the opportunity to take classes that focus on development, but I really think that every aspect of biology starts with developmental biology.

**Finally, what do you do out of the lab to get away from your work?**

This might sound cliché for a French guy, but I do enjoy cooking a lot. It brings me back to my initial passion for science.

When visiting a new city or country, I am always on the hunt for a nice restaurant where I connect and learn about the culture through food.

I also run a lot. I've done several half marathons and I was most of the way through training for a full marathon when COVID hit and they cancelled the event, and at that point I thought 'no, never again'. I might change my mind at some point because I like the freedom you feel while running. And in the last few years, I started climbing. Like running, it is a mental challenge to make it to the end. Sometimes, it feels like a puzzle – trying to balance your body properly to reach the next hold – it's a great way to switch off and the climbing community is really friendly.

Loic Fort was interviewed by Katherine Brown, Executive Editor at Development. This piece has been edited and condensed with approval from the interviewee.