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INTERVIEW

Transitions in development – an interview with Alberto Roselló-Díez

Helen L. Zenner*,‡

Alberto Roselló-Díez is a Group Leader at the Australian Regenerative Medicine Institute, Monash University. His lab is developing new tools to ask fundamental questions about limb development. We met with Alberto over Teams to discuss his career, his transition to becoming a group leader and his research plans.

Let's start at the beginning. When did you first become interested in science?

Ever since I can remember. Both my parents are biologists, so I grew up in an environment where they could answer all my questions about animals or anything in science. That kind of positive feedback was really crucial. My interests evolved over time; first, I wanted to be an astronaut, then a nuclear physicist and then a chemist and, finally, since they are both biologists, I guess biology won!

Were your parents also developmental biologists?

No, they were high school teachers, so they know a little bit about everything, but mainly biology and geology. My mother actually started her PhD when I was in high school, so I got to see her dissertation; that was really cool.

Did this influence how you chose your PhD lab and your research topic?

As an undergraduate, I studied in Zaragoza, a city between Madrid and Barcelona, where my mother was doing her PhD as well. When I was searching for a lab for my own PhD, I looked in Madrid and Barcelona. At that time, I was interested in immunology and visited the Department of Immunology and Oncology at the National Centre for Biotechnology in Madrid. One of the people I was interviewed by was Miguel Torres, who was a colleague, of a colleague, of my mother. He is not an immunologist – he's a developmental biologist – but he was in that department. When chatting with him and discussing the questions he was interested in, I realised that I really liked his approach and the questions he was trying to address: how individual cells coordinate and self-organise to form perfect organs, such as a limb or a heart. I was fascinated by both the questions and the approach, and that's why I decided to go to his lab.

From your PhD in Spain with Dr Miguel Torres, you moved to the Joyner lab in the USA. What was your experience of moving between countries?

In terms of the lab experience, I would say it is very similar in every country and, as you know, I've been in three countries. In terms of lifestyle, that was the big change because almost everything you can imagine is different! For example, the healthcare system – we had to learn how that worked. Even shopping was relatively different, and how bank accounts work. They really like cheques in the USA for some reason! They don't use WhatsApp, they use SMS. Basically, every aspect of life was different, so you have to learn. My wife, who is also a scientist, and I moved together. In our case, we were lucky to find a big Spanish community in New York, so it was relatively easy to blend in.

What did you study during your postdoc with Dr Alexandra Joyner at Memorial Sloan Kettering Cancer Center (New York, USA)?

When I was finishing my PhD on limb development and how the different segments of the limb are established, I started to think about what I wanted to do afterwards. I did something that I would encourage anyone to do, if they can afford it: take three or four weeks of 'vacation' just to think and read about what you want to do. I was advised that if I could come up with my own project for a postdoc, that would be seen positively by both funding bodies and the potential host lab. By the time I was finishing my PhD, I started to think about the next steps of limb development; once the pattern is established, how is the growth of the limbs regulated and coordinated? In particular, I was fascinated by how the left and the right limbs are so equal in size. Around that time, Lewis Wolpert published a paper in PLOS Biology titled 'Arms and the

*Online Editor, Development.

‡Author for correspondence (helen.zenner@biologists.com)

H.L.Z., 0000-0002-8578-9797

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Man: The Problem of Symmetric Growth' (Wolpert, 2010) and he was talking about the same problem. I thought, 'well, that's a nice coincidence' because he was a very big figure in developmental biology. I started to think about how to tackle this problem using some genetic tricks. I developed my own ideas and I proposed a project to several labs in the USA. I decided to join the Joyner lab for two reasons: one, it's a leading lab for new tool development; and two, because of their background in limb development research.

Limb development is a strong theme throughout your career so far – what attracted you to this topic?

Good question! The limbs, the larynx and the brain are perhaps the things that make us humans – in particular our opposable thumb. When I was starting to think about developmental biology, I often wondered, 'how is it that we always have five fingers?' or 'how do we have left and right limbs of the same size?' I think the limb is a fascinating organ, in the sense that it keeps growing while patterning is established. How does the limb update its pattern during growth? I thought this was a fascinating question. Also, the limb is eventually composed of many different tissues: bone, muscle, cartilage, tendon, dermis, fat, etc., which have to remain coordinated as they grow. I thought that was another fascinating process. I am really drawn to challenges, and sometimes challenges can be frustrating, but I guess that's who I am!

Why did you decide to look for group leader positions?

During my PhD, I noticed that I often had my own ideas about how to move a project forward. When I suggested these to my supervisor sometimes they were completely changed, but sometimes they were received well. Of course, I then developed my own project for the postdoc position, and although I didn't fully confirm the hypotheses I had, overall the project worked out very well. This positive reinforcement really motivated me. So I would say, by the end of my PhD, I realised I could be a good group leader and my postdoc experience confirmed this to me.

And how about actively looking for positions, how did that fit into your time as a postdoc?

That was a very complex period because I was developing new tools, and in the mouse that takes a long time. My postdoc was a long one; it was almost six years. The first few years, it was tool development and little else. At some point, I found myself having to apply for group leader positions, maybe a little bit before I would have liked to – before my main papers were out. To maximise my chances of success, I applied to many places, probably around 50. I was working on my paper at the same time, so there were many sleepless nights. Presumably based on future potential rather than publications, I got eight interviews and finally two offers. I was able to secure a position even before my main papers were out, so it worked out, but if I could have had one extra year to do that it would have probably been less stressful.

Did you ever consider a non-academic career path?

Never. My motto was: no plan B!

What was most important to you when choosing a position and why did you choose the Australian Regenerative Medicine Institute at Monash University, Australia?

The main factor was always being able to do the science I wanted to do. Then the second factor would be the social or the lifestyle, especially as we had our first kid whilst in New York. We really like the science system in the USA, but there are some aspects of the lifestyle that we thought were probably better in Europe. We were trying to find a good balance between a good institution for doing my science and raising kids in a more familiar environment. In the end, I got two offers, one in Europe and one in Australia. I really like my colleagues and the kind of science that they do here at the Australian Regenerative Medicine Institute and the platforms that Monash has available. So it was a good combination, but it took some convincing for my wife because it's very far away from Spain, but here we are!

Were there any parts of the application process that surprised you?

What surprised me about the application process was how many different research proposals I had to prepare. Some institutions asked for a two-page proposal; at others it is three or five pages. In some of them you are supposed to include your past research, in others a general research vision, while some cut straight to the chase with just your future project. This meant that even though the research was going to be the same, I had to work on many different documents to say the same things in very different spaces. That took a long, long time; so people should be prepared to have many different versions of their research proposal.

In terms of the interview, a lot of people are afraid of, or have a lot of respect for, the so-called chalk talk, in which you have to explain your future plans to a room full of professors. You have to defend your plans, and you don't know where the conversation will take you. But I actually enjoyed discussing my science and the possibilities so much that in 90% of the cases I really enjoyed that part the most. Also, it meant that, even if I didn't get the position, I still had a good time chatting with potential future colleagues.

Do you think mentorship has been important for your career?

It is definitely crucial; I don't think anyone can really succeed without mentorship. Although I was quite independent from the start, I did listen to advice. I think the main role that mentorship had in my case was opening connections to people, for example having a well-connected mentor who could help me find a new technique or model that I needed, or to introduce me to colleagues at a meeting – if you can remember those times when we could go to conferences in person! Also, mentors helped by suggesting me for a talk or asking for help with peer review.

How was your experience transitioning to a group leader position?

It was the hardest thing I've ever done. I still consider myself to be starting my lab, especially with the COVID-19 pandemic. It feels like it's still gathering momentum. There were too many changes at the same time: moving to a new country, starting in a new institution and having new colleagues. You go from being a master in the lab, where you know where everything is, how it works, to moving to an empty space that you have to fill with people and equipment. The techniques that you were so familiar with, all of a sudden, don't work, and you have to troubleshoot them again. So many new things can be daunting. So, I would recommend having a lot of patience and recognising that not everything has to click in the first few months. Take your time to hire people – don't rush it. It's okay to be alone for a few months, if necessary, because in the end, having the right people is crucial. Every successful PI I have talked with says, 'I was so lucky with my first student or my first research

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assistant'; there is a pattern there! So, take your time and ask for advice.

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What has been your approach to hiring new team members? Has the pandemic impacted this?

We try to advertise as broadly as possible. In our case, Australia is very far from most of the rest of the world, so it is hard to get international applicants. I advertised on the Node, with societies, and via university channels, as well as colleagues and Twitter. Then, in terms of selecting candidates, I asked a couple of other PIs – more experienced PIs – to be involved in the interview process. You should make sure that the people you're trying to hire are interested in what you do, not just that they have seen an open position. They have to be really interested in your lab and what you are doing, otherwise it will not work out. The pandemic definitely had an effect, both at hiring level, as the closed borders restricts the pool of applicants, and at the training level. I had two new people starting in March 2020. As you can imagine, we couldn't do any training because all of a sudden the lab was shut down or had restricted capacity. 2020 was pretty much a lost year in terms of progressing with projects, or training these people.

What are the research themes of your lab now?

There are two main themes. First, studying the recovery after developmental perturbations, or what is called 'catch-up growth', which we can study by altering it. For example, if you alter that growth trajectory by insult or injury and then remove it, you allow for recovery. In many cases, there is fast overgrowth or hypergrowth, to reach that normal trajectory and then, once the normal size for age has been achieved, growth goes back to normal. We are trying to determine which cell populations and molecular pathways are involved in that response. It is giving us some very interesting results. The second theme, which we just started with, is: what are the genetic determinants and epigenetic determinants of limb size? So how mice and rats can have similar genomes but different limb sizes. We are asking whether limb size is affected by the environment of other organs or the external environment. We are developing genetic methods to generate chimeras, such as mouse embryos with limbs formed by rat cells. It's quite a complex experiment, but it's doable. It's been done for other organs, such as the pancreas or the kidney, but we are going to, hopefully, be the first ones to do it with a limb. We hope to find out how these signals from the mouse can affect the development of rat limbs. We'll see whether the developmental tempo affects patterning, and therefore the size of the limb, and we will try to determine what gene regulatory networks are involved. I'm very, very excited about that part!

You have been a researcher in Europe, North America and now in Australia – are there any key differences in either lab life or funding opportunities that you can share?

Funding is the biggest one. In Europe, at least when I was last working there, it used to be the case that bold proposals, with interesting ideas – high risk, high reward – were funded. In the USA, I had to learn to write more feasible proposals, in which everything was more established. There's a saying in the USA – you get the money for the project once the project is done, then you use the money for the next project. In the USA, although it is never easy to get funding, the pot of money is so big, that it is relatively accessible. And then in Australia, it's challenging, and it's becoming more challenging. You can see on Twitter the frustration that many people share; the pot of money is small and it is not growing. The funding that is available is being diverted towards more applied research and basic or fundamental research is really suffering. For people transitioning to their first independent position, the success rate is abysmal. There is a huge concern here about where research funding is going. We were very lucky last year to get a big grant from the government, but who knows what will happen in a couple of years' time.

Related to that, recently there has been some discussion on Twitter about including preprints as references in your grants, can you tell us more about that?

Oh yes, that was a huge thing. The Australian Research Council, for some reason, decided not to allow preprints to be referenced at any place in the proposal. It was kind of hidden in the guidelines, but then they were really enforcing it. This meant there were many projects considered ineligible, and then there was huge outrage. With preprints being so important nowadays, that stance was surprising, but, luckily, they reconsidered their position so for the new applications, they will allow preprints to be referenced.

You have published both a first author and a corresponding author paper in Development, do you think that publishing in our journal helped your career in any way?

Yes, definitely. It's one of the two or three main journals in developmental biology. It's always a reference journal for me and for my colleagues. That first author paper you mentioned (Roselló-Díez et al., 2014) ended up being cited and referenced in the Faculty of 1000 (now Faculty Opinions; https://facultyopinions.com/prime/718299574). It was included in Gilbert's Developmental Biology textbook (Gilbert and Barresi, 2016), so I think that was a really good outcome. The corresponding author paper (Ahmadzadeh et al., 2020) is about the new technologies that we have developed. I have had many requests, both in my lab and my former supervisor's lab, for these mouse lines or related vectors. So, I think publishing in Development has been really good for advertising our technologies.

You've been involved with science communication, posting on both our community site, the Node, and preLights. What prompted you to participate and would you recommend it to other early career researchers?

Even though doing research is my passion, I think that communication is really important. We have society trusting us with public money, so we should explain our research to a broader community. Of course, preLights is quite specialised, but everything we can do to spread the word of the research is important. Also, in the case of preLights, it's actually quite fun to get in contact with the people involved and tell their stories. In terms of other stories, like the one I wrote for the Node, I tried to focus more on the personal aspect of developing a project from start to finish, which gets lost when you publish your paper. For people struggling in the lab, it might be really refreshing to read those challenging stories and how problems were overcome. In terms of whether I would recommend it, definitely! Of course, as an early career researcher, you're always busy with developing your own projects, trying to look into the next step or developing your family, but you should still aim to fit it in if possible.

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

I try to apply science to everything I do. I am really into role-playing games (or used to be – I don't have the time anymore) and whenever I was playing those games, I always tried to apply the physics that I remembered from the real world. Or when I'm in the lab, I always try to do my calculations mentally. I really don't like to use calculators. I try to teach my students how to do mental approximation first and then how to approach the final figure. I think you always have to keep challenging yourself!

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