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INTERVIEW

An interview with Roberto Mayor

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Roberto Mayor is Professor of Developmental and Cellular Neurobiology at University College London. Elected an EMBO member in 2019 and a former International Scholar of the Howard Hughes Medical Institute, his lab works on the development of the neural crest, in particular its induction and migration. We met Roberto in Buenos Aires at the tenth biennial meeting of the Latin American Society for Developmental Biology (LASDB, the society he founded in 2001), and discussed the role serendipity has played in his career, why we need a more holistic view of the cell during development, and the challenges and potential of science in Latin America.

Let's go back to the beginning: when did you first become interested in science, and biology in particular, in the first place?

When I was a kid I really liked animals, and had all kinds of them in my house. They weren't really pets as I didn't like the concept of keeping pets, but I just really liked interacting with them. At school, I did well in physics, chemistry and biology, and then when I was around 11 I read the book 'Microbe Hunters' by Paul de Kruif that was very influential. It was a story of all the people who discovered microbes through history and how they did it, and I was very impressed: they were so dedicated and passionate about what they were doing, and had so many difficulties that, in the end, there was a real sense of achievement in their discoveries. I think I became interested in science as a possibility for the future at that point, but in my family there was no one in a science-related job – it was not immediately obvious to me that this profession even existed. I started to do some research – in the days before the internet – and I found that in Chile at that time, most of the scientists doing biology were coming from a career that was called Biochemistry. So I decided that OK, biochemistry is for me, and went to study it at the University of Chile in Santiago. However, I was initially disappointed because the 'bio' side of things was very small; but I learned a lot of chemistry and physics, which was very useful in the end.

How did you come to find your PhD project and mentor?

It involved a lot of serendipity really: I was studying biochemistry in the Faculty of Pharmacy (which had no biologists in it), and that was during the military government in Chile. This military government liked to do all kinds of experiments with universities, and they decided to merge the Faculty of Pharmacy with another one I didn't know about, the Faculty of Science, as I entered my fourth year. I then had the opportunity to take the biology course with the best biologists in the country at that time, who were at the Faculty of Science. There were two professors in particular, Juan Fernandez and Luis Izquierdo, who were developmental biologists and very inspiring to me; that was when I really decided to become a developmental biologist. I finished my course and was expected to do a thesis, and I did mine in Luis Izquierdo's lab, and ended up staying there for my PhD, working on mouse preimplantation analysis.

Roberto on a recent trip to the south of Argentina, with an elephant seal pup in the background.

Your first paper came from your time in that lab – why were you interested in intercellular connections in preimplantation mouse embryos?

My first paper (Mayor et al., 1989) was actually my undergraduate thesis, and about a process called compaction that takes place in early mammalian embryos. In mice, when the embryo is made of eight cells, each of them looks quite individual, and then suddenly all these eight cells are transformed into one ball of cells that are now indistinguishable. The aim of the project was to study the cytoskeleton during that process of compaction: how does it change? I found something very intriguing – each cell, just before compaction, establishes connections of actin with the other cells in the embryo. We published it in 1989 and recently the same observation was 'rediscovered' using more sophisticated techniques (Fierro-González et al., 2013).

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Development (2020) 147, dev187252. doi:10.1242/dev.187252

You then moved to England and the National Institute of Medical Research at Mill Hill for your postdoc with Mike Sargent – why did you decide to change model organisms, to *Xenopus*?

When I was finishing my PhD, my supervisor made a very good offer to me. If I went abroad for a postdoc, he would offer me a position when I returned, being in charge of his lab. I was just a PhD student so was very impressed, and obviously accepted. I was planning to continue studying mouse preimplantation development, and Martin Johnson, based in Cambridge, UK, had agreed to hire me. I was all ready to go to work with him, and then there was a problem with the approval of my PhD thesis. Acceptance of my thesis was postponed again and again, for so long in fact that I missed the chance to go to Cambridge, and was left without a lab to go to.

But even before this point, I actually had started thinking more broadly about which approaches we should be taking with developmental biology. The genetic approach had obviously been very successful and quite dominant, but my feeling as a PhD student was that the activity of genes alone could not fully explain development. If you want to understand a particular process, for example gastrulation, and then you find that when you mutate gene X that gastrulation fails, some people will be satisfied with the explanation that X controls gastrulation; but I was not. I was interested in how the gene X controls the cellular behaviour that leads to gastrulation.

And then I was incredibly lucky to attend the Embryology Course at the Marine Biology Laboratory in Woods Hole. Two great people were running the *Xenopus* module: John Gerhart and Mark Kirschner. They were very inspiring, and showed me that you could approach development from a cell biological perspective. So when I didn't have a lab to go to, I started to think about switching focus, and was attracted to *Xenopus*. I talked with my supervisor, and while at the beginning he wasn't totally convinced, in the end he was very generous and supportive about the idea. He contacted his good friend Anne McLaren and asked her for advice about a UK *Xenopus* lab. She suggested Jim Smith, whose lab turned out to be full but he in turn put me in contact with Mike Sargent, who happened to have an open position. And in a matter of weeks I was packing my things to move to Mill Hill.

Did you feel a culture shock moving to London?

Not really – I mean I really enjoyed living there, so much so that I came back years later. But the shock was really the science: it was just amazing, and particularly the developmental biology going on in Mill Hill at that time.

Your most-cited paper comes from this time – published in Development and reporting induction of the neural crest. How did this work come about?

Mike Sargent was collaborating with Jim Smith, and both were interested in mesoderm induction and development. Mike had cloned the vertebrate (*Xenopus*) homologue of a gene called snail that was expressed in the mesoderm of *Drosophila* and played a role in mesoderm development. My project was to try to identify the regulatory regions of snail that control its mesodermal expression. It was a very interesting topic because Jim Smith had recently identified one of the first (if not the first) mesoderm inducers – activin. Could we find the regulatory regions of snail that respond to activin?

I did a lot of molecular biology, cloned a lot of genes and regulatory regions, and made a lot of reporter constructs that I injected into the embryo. And I found that, as expected, some constructs produced expression in the mesoderm, but there were also some constructs that produced expression in another population of cells that, at the time, I had no idea as to their identity. Later, we found that these were neural crest cells, and so snail wasn't just mesoderm specific. In parallel at that time, K. Roberts, a rotation student, by chance found a gene that was very similar to snail, that Mike later named slug, and it was also expressed in the neural crest. It much later became famous for its involvement in the migration and EMT of cells both in developmental and cancer contexts.

So then I had to come back to Chile. I talked with Mike and he was still interested in sticking with the mesoderm, while I was very keen on this neural crest story, and that induction paper was actually finished in Chile (Mayor et al., 1995). People had been studying neural crest for many years, but the only way they could recognise where these cells were in the embryo was by labelling and following them. And here we had these genes that labelled exactly where the neural crest would arise – it was very exciting.

Serendipity gives you opportunities, but you have to be ready to take them

And this was another example of serendipity in your career?

Yes, and I think this doesn't just apply to me but to many scientists. The key thing I guess is that serendipity gives you opportunities, but you have to be ready to take them. I could have ignored the neural crest expression, for instance, but thought it was too interesting to overlook.

When you returned to Santiago to establish your own lab, what was the scientific environment like?

I returned in 1993. I was supposed to go back to work in Luis Izquierdo's lab, but he had in fact died in 1992. When I went back to his lab, it was actually my lab, but I really had to start from scratch since the lab had never done molecular biology (just imagine, no pipettes!). It was not easy, but I enjoyed it very much. The main thing I missed was having people to talk to about our work. At that time, I was the only developmental biologist in the whole country who was using molecular biology to understand development.

A little later I had the opportunity to visit the University of Virginia as a Visiting Professor, to learn some embryological techniques in Rob Grainger's lab. When I arrived there after being in Chile for 2 years, it was amazing – finally I could talk to people that could understand me! A few year later I did a mini-sabbatical in Judith Eisen's lab at the University of Oregon, to learn zebrafish work. I also had a great time there learning and talking with other developmental biologists. I think that was the main difference in coming home: the isolation.

And then you came back to England again, moving your lab to UCL – did you always mean to return, and what aspects of neural crest development were you interested in?

As well as being full of fantastic developmental biology, I also felt like the work I was doing was always appreciated in the UK, which made it very attractive to me. And there another person played a very important role – Claudio Stern, who was the director of the Department of Anatomy and Developmental Biology at University College London (UCL) at the time, who offered me the position and was very supportive when I set it up.

In terms of the neural crest, I had always been interested in two questions: how is it induced and how do the cells migrate? Back in Chile, I could only work on induction – even though I was very interested in migration, we didn't have the infrastructure to study it,

Development (2020) 147, dev187252. doi:10.1242/dev.187252

no microscopes to make time-lapse movies, for example. In Chile I worked for nearly 10 years on induction, and we proposed a novel mechanism for how these cells were induced. And when I moved to London, I continued working on induction – and still we're doing a bit on this today – but I could also research the other question of how the cells migrate.

I always believe that in science you have to ask very simple questions in order to get a useful answer, and I had a very simple question: the neural crest cells migrate in a very directional manner, so how do they know which direction to go in? That was my very simple question but in the end the mechanism was very complicated. I'll often ask the students I teach the following question: if you have a group of cells that goes from one position to another in a very directional manner, what mechanism can you propose for this migration? And everyone suggests chemotaxis – there is a chemical gradient that the cells follow. And we, as well as lots of other labs, were looking for this chemoattractant for years, but nobody had ever found it. This led to the possibility that there was an alternative mechanism, and then we observed a phenomenon called contact inhibition of locomotion – when two cells collide, they move away from each other. If you have a group of cells that are confined within a lane, and they exhibit contact inhibition, there is really only one way they can migrate, and we proposed that this is a mechanism to explain the directional migration of the neural crest. Contact inhibition itself had been discovered 60 years ago by Michael Abercrombie, working at UCL, and I was told by Claudio Stern when I started that my lab was in the exact same spot as Abercrombie's! He had found it *in vitro*, but people had thought it was an artefact of culture. We found it was a real phenomenon, in the neural crest of *Xenopus* and also in zebrafish.

You've incorporated modelling and biomechanics in your recent work: does this involve your lab learning new tricks or do you rely on collaboration?

It's a mix of the two really – some things are based on collaboration, others come organically. For example, Carlos Carmona-Fontaine, the student who led the contact inhibition work, published one of our first mathematical models. This model was developed by him – he's a biologist, but he learned how to do modelling to help with the question of directionality. And today, I usually have a postdoc in the lab who can help with the modelling side of things. I don't have that expertise myself, but I can communicate with those who do. I do believe in collaboration – it's very rare to find a person who has the knowledge and expertise in all these different approaches that we use today to understand development.

I always tell my students that the cells are very clever: they know all the biology, all the chemistry, all the mathematics, all the physics to behave and to be happy. The problem is that we as scientists have learned just a small portion of this spectrum. Most of the research in cell biology as applied to development is focused on chemical signals, but I believe that mechanical signals are equally important for the cells. They don't necessarily distinguish a chemical from a mechanical cue, but our research is mainly focused on one and not the other. Collaboration – with biophysicists, for example – will actually give us a better understanding of cell behaviour. We, of course, are very interested in cell behaviour, and so we need the different approaches – mechanics, physics, mathematics, genetics. The lab today is very interdisciplinary and very collaborative.

Is there anything else that keeps the Mayor lab up at night?

One other thing we're very interested in is an idea that really started during my PhD with the observation that, during compaction, you turn eight individual cells into one ball of cells where you can't really distinguish them. We recently published a review in Journal of Cell Science (Shellard and Mayor, 2019) about supracellularity – the idea that it might be better to think of development, or at least some aspects of development, not so much in terms of the activities of individual cells, but based on the activity of groups of cells: the supracellular organisation. In the review we compare two processes that you might consider at first to be completely different. In gastrulation, there is a process called epiboly – cells from the animal pole extend to cover the whole embryo. And there is another process in ascidians that is called ooplasmic segregation – you have a fertilised egg, and some cytoplasm in the animal pole extends to cover the whole embryo. In one case, you have many cells migrating, in the other, you just have one cell, but when you compare the processes they really are not so different. Can we better understand gastrulation as a process occurring in a single unit, instead of as being based on individual cells? There's another example from *Drosophila*, where mutants that do not undergo cellularisation can more or less still gastrulate like a normal embryo. So this is an idea we're particularly interested in now – supracellular organisation.

More broadly, developmental biology is a very exciting field at the moment. Which big questions will dominate in the next decade?

I'll try to answer this in a more objective way, rather than just going with my gut. I recently became Editor in Chief of the journal Mechanisms of Development, and we've been thinking about which direction we want to go in. I asked the publisher to do some analysis – in developmental biology journals, which words are frequently cited today? And we found that forces and mechanics are the most cited words in the field. Biomechanics itself is growing very rapidly, as shown by its increasing citation rate, even faster than epigenetics, for example; but the proportion of biomechanics research that is actually carried out *in vivo* is tiny – I think that is where we have an opportunity for the future. One of the reasons why biomechanics *in vivo* is so difficult is that we haven't had the techniques to measure or modify biomechanical properties in the animal – but now these techniques are coming and developing, and I predict a lot more growth in it. These techniques will help address what I was talking about earlier – the need for a more holistic view of what a cell experiences during development. One problem with just explaining development by chemical signalling is coordination – you have a whole embryo, which can be quite large, and all the cells are doing something at the same time. Mechanics is a very good way to coordinate activity, as mechanical signals can be transmitted almost instantaneously to all the other cells, in contrast to diffusion of a signal, which can take ages!

We're here in Buenos Aires for the LASDB meeting. You founded the LASDB and served as its President from 2003 to 2007 – why did you create the society and how important is the society to Latin American science today?

It was not my idea – it came from a group of students. Twenty years ago I started organising a practical developmental course for Latin American students in Chile (we started in Santiago and more recently we moved it to Quintay). We had the first course in 1999, and in the second iteration, in 2001, the students asked us if we could establish a regional network of developmental biologists. I thought it was a great idea, and I asked Eddy De Robertis, who at the time was the President of the International Society of Developmental Biology, what he thought about it. He said we

Development (2020) 147, dev187252. doi:10.1242/dev.187252

didn't need a network, we needed a society. So we did it, and it was very quick. In January 2003 we had the first meeting, in Chile, and since then it has been very active.

I could give you many, many examples of direct effects of the society on the progress of developmental biology in Latin America, whether in terms of collaborations or papers, for example. It was funny – when we started we said, 'OK, who is doing developmental biology in Argentina, in Mexico, in Bolivia?'. And I had no idea! I didn't know, and nobody really knew, because people were so restricted to their own countries. The first challenge was to find these people, and we ended up with some names to start the society. Now the young people who join the LASDB today would find this unthinkable; the society has really helped to create links, collaborations and friendships across Latin America. In the inauguration of the first LASDB meeting in 2003 I wrote: 'This is an experiment very similar to those performed by each of us in our laboratories. We do not know exactly what will be the outcome of this experiment in the future'. When we created the society, I would never have imagined how far it has gone and the effect it has had on Latin American developmental biology. Latin America is quite big, but the science is quite small. The only way to move forward is to collaborate across borders.

Is there a particular style of science done here?

I don't think so really – there are some great departments and traditions, but I don't think that there's a particular way of doing things, except that it is very challenging. They're asking the same questions that scientists ask in the USA or Europe, but the conditions are much harder: they have to be very creative to solve these problems. They have a lot of difficulties, but they have something that I believe we don't have at similar level elsewhere – the quality of the students. I always say that Latin American students are among the best in the world – one of the reasons may be that they are often very committed to do science from an early age. We just selected students for the next version of the Quintay practical course, and the quality was just amazing – we really struggled to pick the final set.

Do you have any advice for someone considering a career in developmental biology?

All I'd say is to follow your instinct and your passion. I have been very irresponsible in my career, not thinking of jobs or anything like that (though this is probably because I have been so lucky with my opportunities!). I recognise that times are difficult now, but my advice would be that if you really believe in something you can find a way forward. And there might be a limit to how much you can plan out your career, at least from my experience, where my major career transitions have happened through serendipity.

Is there anything Development readers would be surprised to find out about you?

One thing I really like is painting and drawing. I design the posters for our department's seminar series at UCL – for each person who comes I'll read about what they do and try to have a creative response to it. They can be quite abstract, and I really enjoy doing them. I've always enjoyed art and it's one of the reason I love living in London, since there's art everywhere.

References

Fierro-González, J. C., White, M. D., Silva, J. C. and Plachta, N. (2013). Cadherin-dependent filopodia control preimplantation embryo compaction. *Nat. Cell Biol.* **15**, 1424-1433. doi:10.1038/ncb2875

Mayor, R., Pey, R. and Izquierdo, L. (1989). Development of cytoskeletal connections between cells of preimplantation mouse embryos. *Roux Arch. Dev. Biol.* **198**, 233-241. doi:10.1007/BF00375910

Mayor, R., Morgan, R. and Sargent, M. G. (1995). Induction of the prospective neural crest of Xenopus. *Development* **121**, 767-777.

Shellard, A. and Mayor, R. (2019). Supracellular migration - beyond collective cell migration. *J. Cell Sci.* **132**, jcs226142. doi:10.1242/jcs.226142