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INTERVIEW

An interview with Maria Elena Torres-Padilla

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Maria Elena Torres-Padilla is Director of the Institute of Epigenetics and Stem Cells at Helmholtz Zentrum München, Germany. Maria Elena, who studies how cell potency and cell fate are regulated by chromatin-mediated processes, was recently appointed as an Academic Editor at Development. We caught up with Maria Elena at a recent conference to find out more about her background, her research and her thoughts on the ties between the chromatin and developmental biology fields.

So let's start right from the beginning: what first got you interested in science?

I guess what first got me interested in science was a curiosity to find out new things and to understand how things work. I had a doubt about whether I wanted to study medicine or biology, but I was sure that I wanted to study life sciences and pursue research. I ended up doing biology because I wanted to have a broader picture of life, so to say.

After graduating in Mexico, you moved to France to embark on your PhD – how and why did you choose France, and was this an easy move?

I think I was 13 years old when someone asked me 'why are you studying French?' and I said it was because I want to do a PhD at the Pasteur Institute! I guess the Pasteur was a very well-renowned institution so that's why I was so focussed on going there. But I also thought that if I am going to move from one place to another, I want to profit from the culture, history and language of that place. France was a very attractive possibility for that. So I targeted a lab at the Pasteur that was interested in gene regulation in response to signalling. I joined the lab of Mary Weiss and ended up working on hormone receptors and how they could mediate different outputs in terms of gene regulation. At this time, the distillation of histone modifications was starting to be very trendy, and I ended up being very interested in histones because it turned out that the nuclear receptors I was studying were able to recruit different histone-modifying enzymes. From there, I basically thought 'OK, this is very cool because instead of just looking at one transcription factor, I can look globally at the (epi)genome'. So that really propelled my interest in chromatin and epigenetic regulation, and I realised that I wanted to take a more global approach to looking into how gene regulation can actually lead to cell fate changes.

You then moved from France to the UK (to The Gurdon Institute in Cambridge) for your post-doc, where you became interested in the epigenetic control of early mouse embryo development. How did you find your time in the UK?

I very much enjoyed the pragmatism of British scientists, and the fact that people seemed uncomplicated in general. I think that really left an imprint on the way I think and do science now. The environment at the Gurdon Institute was also just fantastic. There were leaders in the field for many different fields, so I learned a lot. But that also put a lot of pressure on me because I realised that if I could not make it there, I would never make it! So it was not an easy time. I was also trying to bring together two fields that, at that time, were not really together and I think I made a lot of mistakes in that sense. But in the end I was very happy with how things worked out, and with the scientists I managed to meet. And I really miss British beer!

My time in Cambridge also made me realise that there were gaps in the approaches and the expectations of the two fields. I would go to chromatin meetings and they would say, 'Well, that's all fine but you're not doing any biochemistry', and I would go to developmental biology meetings and they would say 'Well, that's good but you need to do the genetics'. I was in the middle of fields for quite some time. I wanted to find a place where there was strong transcriptional biochemistry expertise, but also mouse expertise. And, Strasbourg was one of those places so I ended up going there. I did a two-year postdoc with Laszlo Tora, who is an expert in biochemistry, and applied for group leader positions at the same time.

So then, having been exposed to the fields of developmental biology, chromatin biology and biochemistry, what was your aim when you started up your group? What was the big question you set out to answer?

I wanted to explore cellular plasticity and how it is regulated by chromatin-related processes by using novel and different approaches to what people had used before. Specifically, I wanted to understand

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how chromatin regulation enables the establishment of totipotency during epigenetic reprogramming, and how totipotency is slowly lost. This is a fundamental cellular state in development, at which cells can form a new being on their own, and therefore has fantastic potential. At the same time, we know very little about the mechanisms that sustain this state, causally, so there is still a lot to do! There have been quite a lot of challenges, though. For example, what's the readout for totipotency, what are the quality standards, how do we test for it? These aren't easy questions to answer, and the systems that we use to address these questions also aren't easy to work with.

Moving on to your model system, you've used the pre-implantation embryo as a model for many years now. What are the advantages and disadvantages of using this system?

I think the main advantage is that this is the only model system in which totipotency truly exists in mammals. We can really follow epigenetic reprogramming from start to finish, exploring its whole conceptual endeavour.

But the disadvantage is that it's hard to gain mechanistic insight because we can't really do proper biochemistry. It is very difficult to do beautiful and clean biochemistry with low-input material, so we've had to explore different approaches to address our questions. Genomics, for example, is becoming very popular, and a lot of work (by us and many other colleagues) has started to build on this. But many of these studies, ours included, have still been limited due to the sensitivity of low-input approaches. But as these approaches improve and evolve, I think we can start to build up a stronger case.

Can you tell us more about the 2-cell like (2C) cells that you're using now?

We first became interested in '2-cell-like cells' or '2C' cells – cells that resemble the blastomeres of the 2-cell-stage mouse embryo – because we were looking for a biochemically tractable model that we could use to address at least some of the issues that we were exploring with regard to the totipotency window *in vivo*. These cells were originally identified by Todd Macfarlan and Sam Pfaff as cells that arise spontaneously in murine embryonic stem cell cultures, but at a very low proportion: only around 0.2% of a given culture will actually be 2C cells. So I am very interested in them because they provide an additional system that we can use to tackle cellular plasticity, primarily because they recapitulate many molecular and cellular features of the blastomeres of the 2-cell-stage embryo. But there is still a lot of work to do to characterise these cells properly. What exactly are they? What can we do with them? To what extent do they recapitulate the features of the early embryo and to what extent do they not? So, for now, there's lots of characterisation to be done. Perhaps then we can actually perturb the system and ask if it responds in a similar manner as the embryo and vice versa. It's quite interesting to go back and forth between the two systems in the lab; it is a real strength.

As well as running your own group, you set up the Institute of Epigenetics and Stem Cells at Helmholtz Zentrum München – what was the incentive behind this and, having worked at lots of different institutes across the world, what did you see as the key things that were needed to establish a successful institute?

The people that you recruit are key. It's the same as in your lab: one has to recruit better people than oneself to really get things working at the level that one would like them to work, and I think this is when science starts being fun. I also think the critical mass of the people that you bring together in an institute is very important. This is something that became very obvious to me during my time at the Gurdon Institute – there was a critical mass of outstanding people. I think that's very important for creativity and for really fostering an environment of leadership and empowering the younger generation. When people are very good, the interactions come and so does good science. I think good scientists also come with a lot of flexibility; they are by nature curious about science.

The focus of what we are doing in the institute is centred on epigenetics and cellular plasticity at large. But what we do is very broad – we work on nuclear organisation, on heterochromatin formation, on transposons and on pluripotency, but also on cell fate modelling, genome stability and transcription-replication conflicts, and of course on reprogramming! I think having this broad outlook will help us to answer bigger questions and better understand how the chromatin landscape in general changes during cell fate transitions.

Last year, the German Stem Cell Network (GSCN) awarded you with their annual 'GSCN Female Scientist Award' – can you tell us how you felt to receive this award and more about your thoughts on the challenges that women in science face?

I always think that I have not done enough to deserve these types of recognition so, of course, I was very surprised and honoured to be given the award. What I think is important for science nowadays is to create a truly inclusive, respectful environment: that everybody has the same choices and opportunities. It should not matter if they are a man or a woman, or from the northern or the southern hemisphere, or from a certain minority: I think our task is to really make sure that we teach the future generation that everybody should have the same chances. We need to create an environment that achieves that. Likewise, creating awareness of disrespectful environments is very important. People often ask me if I have been discriminated against as a woman, but I think I have been more discriminated against as a latino (Mexican) than as a woman, but again, this is just my perception. We have to raise strong people who are able to respect the person sitting next to them, whether the person is a woman, a man, or from a different background to them.

You've recently joined Development as one of our Academic Editors – what do you hope to achieve in this new position?

I think one aim is probably to promote the field of research that I've been working on because I find it very exciting, because I think it deserves attention, and because there are still many, many questions to be answered. I hope that by bringing some combined expertise in developmental biology and chromatin biology, and also different ways of looking at a question, I can help the field to keep making contributions to developmental biology.

In addition, a lot of questions in the chromatin field are actually developmentally driven, or have some sort of developmental biology underpinning them, yet the people studying these questions sometimes do not consider their work to fall into the category of developmental biology. I think this is a misperception that needs to be changed – that 'development' is not just embryology. It can – and has to be – molecular biology on developmental questions. For example, some of the high-throughput sequencing studies or transcriptomic studies that we've heard about at this meeting have been applied to embryonic cells. Of course, you can also do that using cultured cells, but if you have a phenotypic outcome that you can actually see is important for a developmental process, you can decipher the temporal sequence of events that are necessary for driving this outcome. However, although I work on a developmentally related question, this is not to say that I am not interested in *in vitro* studies because without

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those we cannot understand what is going on in the embryo. Basically, I think that a combination of different model organisms or systems, or complementary approaches, is really important.

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What's your advice for young researchers considering a career in developmental biology?

I think you really have to enjoy what you are doing. Obviously, you have to work hard but it is important that you picture yourself as unique in terms of what you want to do and what questions you want to address. Sometimes it's important to step back and ask yourself 'What can I actually contribute that has not been done before?' Obviously, you cannot do that without good people in the lab and I repeat what I said before: try to recruit (and be surrounded by) people who are much better than you.

Finally, is there anything that Development readers might be surprised to find out about you?

I don't know – I think I am a rather boring person! I speak very fast, although I don't think this is surprising, or interesting, and I wanted to be an astronaut when I was a child. I actually asked my lab what they thought my answer to this question should be and this is what they said: that I am allergic to mice, that my sense of direction is pretty bad but I still manage to travel the world attending conferences and meetings, and that I am interested in policy making and politics, sometimes with a few drastic views. Apparently the fact that I love both British ales AND French wine is also unusual!