

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Jean-Léon Maître

Jean-Léon Maître studied biology at the University of Bordeaux, France, and then joined the laboratory of Carl-Philipp Heisenberg at the Max Planck Institute for Cell Biology and Genetics (Dresden, Germany) and the Institute of Science and Technology Austria (Klosterneuburg, Austria) for his PhD on cell cortex tension and cell adhesion during zebrafish gastrulation. In 2013, Jean-Léon moved to the EMBL in Heidelberg, Germany, to work as a postdoc with a Marie Curie IntraEuropean and EMBO Long-Term Fellowship with Takashi Hiragi on the mechanics of the pre-implantation embryo in the mouse. He established his own research group as a CNRS researcher at the Institut Curie (Paris, France) in the Genetics and Developmental Biology unit in 2016 and received an ERC Starting Grant in 2017. Jean-Léon's research group is interested in mammalian pre-implantation development, with a focus on cell mechanics and cell–cell interactions.

What inspired you to become a scientist?

I have always been curious about science in general, but it took me a very long time to figure out a career path. At university in Bordeaux, I didn't really know where I wanted to go or what I wanted to do. My family does not have a science background. Both of my parents were accountants, which is probably one of the most boring jobs I have ever seen! Also, at first I didn't have very good grades – I was not a very good student and I never thought I could make it. But then things just started to work out: I got interested in biology progressively and by year three of university, I realised that I was really passionate about it and decided that research in a lab was what I wanted to do.

Do you feel that the French education system allowed for your 'delayed vocation'?

I feel that one great aspect of the French system is that you don't have to be very mature early on or to make firm decisions – when you're 15 years old, your future is not locked in. You get your high school degree and you can go anywhere you want – whether your grades are quite bad or very good, they'll let you into university. It's somewhat crazy that there's so little selection, but it allows people who are late in finding out what they want to do to still get a shot. However, I wouldn't recommend to anyone to follow this kind of path on purpose – instead, get good grades, study and if you can find out what you want early, do it; I just think it's good that this opportunity is still there for the late bloomers.

How did you end up studying cell–cell interactions in early embryonic development?

John Wallingford (University of Austin, Texas) recently wrote a very nice piece on developmental biology and he said that what gets him out of bed in the morning is *Xenopus* gastrulation. I totally relate to that. What gets me up in the morning is this fascination for the embryo. I can actually remember the first time I saw a time-lapse of an embryo developing, and this just got me straight away. I was very lucky to experience my first time in a lab in the research group



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of Alfonso Martinez Arias (University of Cambridge, UK). His research is dedicated to embryonic development and he is very talented in transmitting his love and passion for it. When I was in his lab, everything was just super interesting and I knew then I wanted to study development. It's a basic and general approach to fundamental biology that I love. This is also an aspect that I like about the Genetics and Developmental Biology department at the Institut Curie: we're dedicated to studying embryonic development – whatever the question, whatever the species.

What questions are your lab trying to answer just now?

We are looking into the early development of mammals; at the moment, we are mostly working with mouse embryos. As we are focusing on pre-implantation development, we are getting our hands on human embryos as well, and we will be looking into working with other mammalian embryos like cow, rabbit, pig, and, in the long term, maybe marsupials. Pre-implantation development finishes with the formation of the blastocyst, which is a structure that has different cell types including extraembryonic tissues that form the placenta and a cluster of cells that will make all of the cells of the mammalian body. We are looking into the architecture of this structure and how you establish it; without proper blastocyst architecture, you don't differentiate cell lineages, you don't implant and embryonic development fails. Now, if you want to shape something, you need

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Jean-Léon enjoying play time with his son Theodor. Photo: Julia Rönsch.

to apply forces, so we are looking into the mechanics of this process and those forces, which are produced by proteins. That's mostly the cytoskeleton and adhesion molecules, but we recently got pretty interested in another type of force generator, which is pressure from the fluid. This includes the entire machinery that builds osmotic gradients and the machinery that makes sure that epithelia are tight and can keep fluid in different compartments and separate the composition in compartments. Animal cells are able to build osmotic pressures and start to draw water and push with hydrostatic forces, just like in plants, which use this force generator a lot. It has been previously explored in pre-implantation development, but we got interested when we noticed that this pressure of the fluid could destroy the tissue. Cell-cell contacts are taken apart and the tissue has to somehow stay organised and repair itself to control the fracture. This is the kind of processes we're looking into – how the cytoskeleton, adhesion molecules and the forces exerted by fluids come together to shape an embryo. Studying forces is one of the coolest things in biological research – you can work with more or less any species and poke it in different ways, and, importantly, the absolute values that force measurements provide allow you to compare forces on cells of a different tissue or species. We mostly use micro-pipette aspiration, which is a way to do arm wrestling with your sample without damaging it.

You mentioned your recent work on hydraulic fracturing of cell-cell contacts. How does the embryo control directionality in this process to establish its axis?

We are exploring this now and there's still a lot to study. What we have done so far is we have tuned adhesion and contractility. For adhesion, the idea is that the fluid coming in between the cells will

fracture the tissue; it is reasonable to assume that the fluid will mostly break contacts between cells that have fewer adhesion molecules. And it works – you can tune adhesion between the cells and this will direct the fluid. Patterning adhesion positions the lumen of the embryo. On top of that, the fluid surrounding the cells and the cells themselves are under pressure, and different cell types have different pressures. The cells will push back onto the fluid differently and so by patterning the pressure of the cell through modulation of, for example, actomyosin contractility, you can direct the fluid as well because the cell will, more or less, push onto the fluid. However, there are other aspects that might control directionality that we haven't touched at all; for example, local pumping of fluid and ions. You could pattern the ion channels and basically open the tap on one side of the embryo and see what the consequences are, which is something we are planning to do.

“Studying forces is one of the coolest things in biological research...”

With this in mind, do you feel that you are influenced by material science to answer questions in developmental and cell biology?

I see our research aligned with the philosophy or approach to try to understand a biological phenomenon with quantitative methods giving out numbers followed by a physical unit of measurement. If you consider the human embryo as a material, you start to ask questions in a different way. Obviously, you have this philosophical dilemma to consider the human embryo as a material – it sounds weird, right? It's not a brick. But you can actually start to understand things differently if you take this perspective, and there's a lot of work on the material properties of cells. For example, our work on fracking of the embryo was very much inspired by the research of Xavier Trepat (IBEC, Barcelona). His research group published on hydraulic fracturing of epithelial cells in a monolayer and their approach was one a material scientist would choose. We get very inspired by work of this kind – much of it was pioneered at the Institut Curie, actually, thanks to Pierre-Gilles de Gennes who applied soft matter physics concepts to living matter.

Are you still doing experiments yourself?

I do enjoy being at the bench and doing experiments and I wish I could do it more often. However, when we started the lab, at some point I realised that by running my own experiments, I would essentially be stealing one of my students' time slot on the microscope. So now, while they do the experiments, I can do something else that is useful for the team and use our time more efficiently. You hire people because they are really good at thinking about their projects and doing experiments and you want to spare them all the administrative issues, which are left to you so that they don't have to do it.

What challenges did you face when starting your own lab that you didn't expect?

I felt I was very prepared and I had anticipated many of the obvious challenges; I don't think I knew how to handle them, but I knew they would happen. One thing I didn't expect was the reverse cultural shock of coming back to France. I lived abroad for over 10 years in Germany, the UK and Austria and they are all very comparable to France, with subtle differences. When you're away from your home country for some time you start idealising it a bit and when you come back it actually feels very different. There was stuff that I just

was not prepared for, like the summer break. The French summer break is nuts! We moved back to France at the end of July, arriving with a young child and trying to settle – in August, everything is shut. You cannot do anything. There is zero administration running, and I did not anticipate this. It was an unexpected challenge to not know how this place that is my home works.

What is the most important advice you would give to someone about to start their own lab?

Many people told me that you have to learn to say no, and not to take every opportunity that is coming. This applies to hiring someone for the lab when it seems this person could do the job but you're not sure. Learning how to say no is difficult. You don't want to turn down opportunities and/or people. I think I say yes way too often, so I don't feel like I actually learned how to say no; but I've been given this advice many times and I think it's important. You can quickly get overloaded by opportunities.

How do you get the most out of the meetings you attend, particularly in the early stages of your career?

I definitely go to many conferences, and give many seminars. I think it's important to show yourself if you want to recruit people. I met Julien, the first postdoc who joined the lab, at a conference. Also, the work we published together wouldn't have gone so smoothly and quickly to publication if I had not crash-tested this study several times in front of the community. It might sound trivial, but research is a collective effort now. Not just one person in the lab, not just one lab – it's a community. It is only through sharing and discussing ideas that they somehow take shape. We discuss projects that are running in the lab with people in the field. That is how we function. I feel like you have to bounce the ideas off as many brains as possible.

What are your thoughts on preprints and data sharing?

We put the manuscript of our recent work on hydraulic fracturing onto bioRxiv right away. Also, we collected all the data and images that were used for the analysis; we did not just provide the raw numbers that we had measured, we also provided the images. There is plenty of information out there and it's free to download. You don't have to ask us, you don't have to type in a password, we don't record any of it. If you want, you can go and download these raw data from the microscope now and analyse them in the way you

want. I feel this has been working really well for other fields, for example in bioinformatics, and the community working on tissue mechanics or on pre-implantation development is friendly enough to allow this. Maybe things would be different if we were in a more competitive community, but this is the current philosophy of the lab. It's quite some work to prepare the data, and make them clean enough for everyone to understand them when accessing them, but I want this to become the trend. We're in an age of transparency. I feel like it's the way forward.

What is the best science-related advice you ever received?

One piece of advice I got from my PhD supervisor Carl-Philipp Heisenberg was that sometimes it's useful to look at the data and write one abstract every day. Same data, different abstracts, to try to spin the story in a different way. I don't write an abstract every day, but I like to think about the best arrangement of the data. This can be tough. It can mean cutting deep into experiments that you've done and just throwing them out of the manuscript because they don't fit with the narrative. Not because they are not true, just because they are not interesting or relevant for the narrative. For my PhD work, it was heart-breaking to not use so much of the data I had collected. I felt that they were so interesting, but they just didn't fit with the story of the paper. Telling stories is fun. As I said, I was very late in realising what I like to do in life, but this is one of the things. And it's globally true now that I have a kid – telling stories is great. If the story is based on facts... even better! [laughs]

“...research is a collective effort now...”

Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

I have a child now, so my hobby is my kid. And hanging out with friends in Paris, that's what I do. I've never lived in Paris before, and I'm having a harder time getting used to Paris than France. Paris is a very large and dense city and I've always lived in smaller cities. That feels very different. I'm not used to it yet, but there are many fun aspects to it.

Jean-Léon Maître was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.