

CELL SCIENTISTS TO WATCH

Cell scientist to watch – Meritxell Huch

After completing her BSc in pharmacology at University of Barcelona, Spain, Meritxell Huch pursued her PhD in the laboratory of Cristina Fillat at the Centre for Genomic Regulation (CRG) in Barcelona. Wanting to move into more basic research, Meri trained as a postdoc with Hans Clevers at the Hubrecht Institute in the Netherlands. In her postdoctoral research, she successfully established a liver organoid culture that earned her the National Centre for Replacement, Refinement and Reduction of Animals in Research (NC3Rs) prize in 2013. Meri joined the Gurdon Institute in February 2014 and is currently a Wellcome Trust Sir Henry Dale Research Fellow. She is interested in the mechanisms responsible for adult tissue regeneration in the liver and the pancreas, particularly in identifying stem cell populations that respond to damage and the intracellular mechanisms regulating their activation.

What inspired you to become a scientist?

The first thing I recall is that, as a child, I could not understand how an aspirin worked; how does this pill know that it has to go to the place that is painful and do its job? That puzzled me so much that I decided to study pharmacology. What pushed me into research is that I always wanted to understand more-and-more how things work, and the lectures were not enough to cover my curiosity in that regard.

What motivates you now?

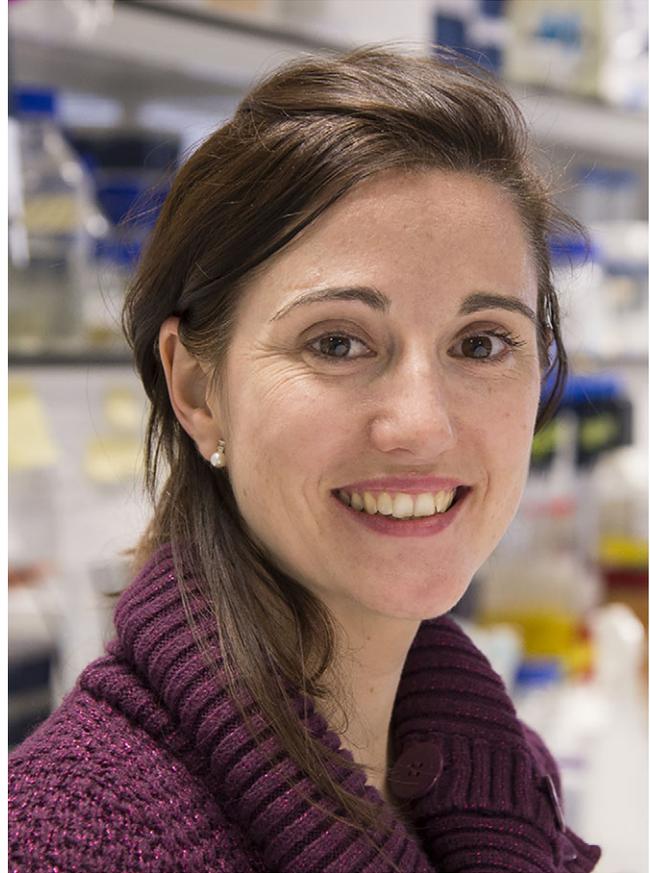
Every time you do an experiment, you suddenly realise that it actually brings you to another question. So you find something out, but it's never complete – there's always another question you want to answer. It's this constant curiosity of trying to understand everything as a whole, when you know that actually it will be very difficult.

What is the research focus of your lab?

The focus of my lab is mainly tissue regeneration. We use the liver, as it has huge potential for regeneration, and sometimes we use the pancreas for the opposite reason – it has very little regenerative capacity in an adult. Both organs come from the same endoderm progenitor cells, which is intriguing by itself – how can they generate these two organs with completely different functions and with completely different regenerative capacity? So one part of my lab is trying to understand tissue regeneration through the regulatory mechanisms that drive the activation of this process, and the other part is trying to model liver diseases using organoid cultures that I developed during my postdoc. This is a 3D culture system that allows the long-term expansion of liver cells *in vitro*. There is also one person in my lab who is asking these questions in the pancreas field. I find it very intriguing that the pancreas can activate the proliferation response, but these cells will rarely differentiate into functional cells. It is the opposite for liver cells, and we're trying to understand why this happens.

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What elements, inside or outside the lab, have been key to your success so far?

I'm a very persistent person; I just keep going until I understand something, which means that I can stay in the lab until midnight and I don't even realise the time. I also had very good mentors during my PhD and postdoc. Cristina, my PhD mentor, opened my mind to seeing things and asking questions that I hadn't thought about. Hans, my postdoc adviser, taught me how to ask the question that is important at the moment that it is important. My husband has also been a key to my success. He is my angel, constantly giving me support, and I would not have managed without him. Of course, my parents also played an important role: when I was a kid, my father once told me: "it doesn't matter what you want to be, an actress, a ballerina, a scientist or a musician, but whatever you do, just do it well and do it from the bottom of your heart" and that was one of the best pieces of advice I ever heard.

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

The surprising challenge was that the UK has a lot of regulations. Maybe I didn't notice them in The Netherlands since I was a postdoc and in an established lab, so all the regulations on how to work with human material or with mice were already in place. Here, I had to set it up from scratch. It was even harder because the institute wasn't working much with human tissue and I'm working with liver, which has additional implications, like potential pathogens (although we don't actually accept any tissue from infected patients). It took a lot of educating myself and my colleagues about these things, and sometimes I found it exhausting. Now, after having all these regulatory issues taken care of, answering the questions we are interested in is the biggest challenge, but that is how it should be; at the end of the day, we are scientists because we try to understand the world around us.

What challenges do you think you will face in the near future?

One challenge is to be fast, and a related challenge, one I will probably face soon, is funding. If you don't get a publication, you don't get funding, and to get a publication, you have to be fast and avoid being scooped. At the end, the one that gets recognised is the one that got there first, but as a small lab it's very difficult to be fast. You don't have the infrastructure that big labs do, with lots of technicians, postdocs and PhD students. There are also so many brains in the world that at least one other person could be thinking of the same types of questions as you. If you knew the person, you could try to collaborate, but if not, you are in a race with someone who might not even exist. So you need to be fast, and you need funding, good people and all your energy and the will to understand the questions you have.

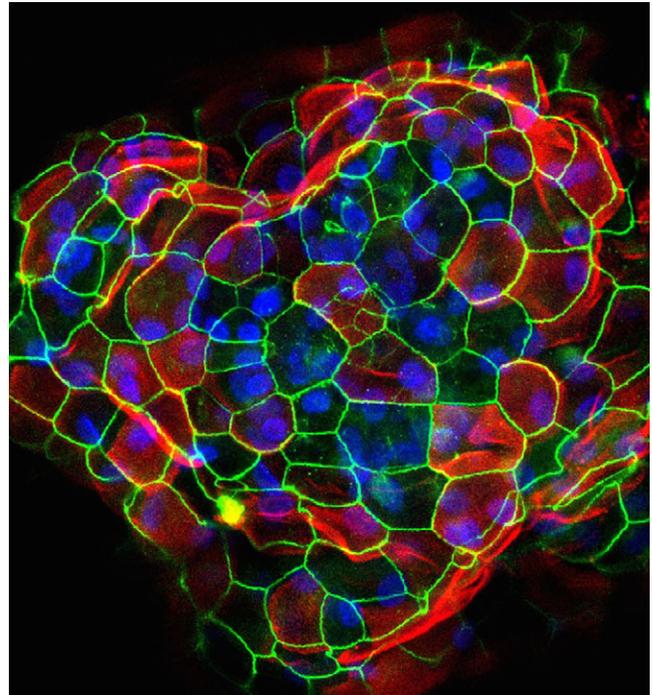
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What is your advice on establishing successful collaborations?

Collaborations are not easy whether you are young or established, although when you're established, you have a reputation, which is like your business card, so when you go to someone they will want to collaborate with you. But when you're starting out, nobody knows you. People may know me because of the NC3R prize and papers, but they still don't know me as a person. They don't know if I'm a good collaborator, and establishing this trust is not easy. I've also been contacted by many PIs who want to use the system we have, and I haven't always had the impression that it was mutually beneficial. My advice is that it's good to collaborate with someone who is not completely in your field, but who has a huge enthusiasm for science and loves what you're doing. You must admire what they're doing as well. It's also good to have a collaborator at the same level.

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

The best advice I got was from Hans, which is that you have to do your best with the people that you have. Sometimes, the first time you hire, you think that the person is a clone of yourself, but it will never be the case. It's a very common error that I also made in the beginning. Learning someone's best skills is the most difficult part of being a supervisor. So try to identify people's strengths and play in that direction, so that they can develop their maximum potential and grow, which will allow your lab to grow at the same time.



Liver organoid. Immunofluorescence image of a 3D human liver organoid stained with ZO1 (green), albumin (red) and dapi (blue). Note the polygonal shape of the cells characteristic of hepatocytes.

Do you still do experiments in the lab?

Yes, whenever I can, although it tends to be less than what I would like to do. But I have a very good example in this institute, because John Gurdon does many of his own experiments – I see him walking around with his white ice box. I definitely want to follow him as a model. I also like to see the raw data and I like to understand how the experiment has been done. I would not like to arrive at a point when there is a technique in my lab that I don't understand, and I think the only way is to stay in the lab.

How do you balance going to meetings with being in the lab?

That's extremely difficult. I get invited to several meetings, and most of them I cannot say 'no' to, because it's considered an important meeting, but I decided that I'm not going to a meeting more than once a month unless it's essential, because otherwise I would never be in the lab. But deciding when to go and when not to go is a very difficult task. As a young PI, you need to know what other people are doing, and despite the fact that people tend to present already published or at least accepted data, there are always several people who will present unpublished data. But I've sometimes been to meetings that are too far away from what we do. Knowing when my time investment is worth it is still a learning process.

How do you achieve a work-life balance, especially at the early stages of having your own lab?

Ah, it's impossible! [laughs] I think at the beginning it's difficult, because you have a small lab, you want things to move forward, but you are used to a different pace from your postdoc and you can't match even half of that speed. You think: 'if I did it by myself, I would be here,' but the truth is: 'if I did it by myself in my former lab, then I would be here. But if I do it by myself in my own lab, I may speed it up a bit more, but I would still not be there.' That means you have to put a lot of time into the lab. I've been lucky that I've managed to recruit good people whom I can trust. Although I

have a bit more work–life balance now, I still feel that the lab needs me a lot. This feeling will never disappear, but at some point you learn how to achieve a balance.

Could you tell us something about yourself that you wouldn't put on your CV?

There's a lab story from my PhD. My lab mates said that they would never tell me when they were going for lunch, because whenever they said "we are going in 5 min" I would say "I will be ready", and I would never be ready. There was always some extra experiment I

wanted to do. In the beginning they would wait for me, and sometimes they waited for half an hour! They also said "you are like Einstein, your time stretches! Your 5 min are always at least 30". At some point they decided they would just go, and I could join them if I could. And I'm still the same, so people in my group just come and say "we're going for lunch" and then they just go.

Merixell Huch was interviewed by Anna Bobrowska, Editorial Intern at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.