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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Prisca Liberali

Prisca Liberali studied chemistry at Università degli Studi di Roma 'La Sapienza' in Rome, Italy. She then pursued her PhD in physical chemistry, studying membrane dynamics and trafficking with Daniela Corda and Alberto Luini at Fondazioni Mario Negri Sud. Afterwards, Prisca joined Lucas Pelkmans' research group at ETH in Zurich and at the University of Zurich, Switzerland in 2008 for her postdoctoral work on genetic interactions and regulatory networks in membrane trafficking, making use of quantitative biology approaches. In 2015, Prisca became an Assistant Professor at the University of Basel, Switzerland while also starting her own research group at the Friedrich Miescher Institute for Biomedical Research (FMI) in Basel. She was awarded an ERC Starting Grant in 2016 and was selected as an EMBO Young Investigator in 2019. Her lab focuses on the collective characteristics of multicellular systems and how patterning can arise from single-cell properties and behaviour. Her research group uses experimental and theoretical analysis to address the cellular heterogeneity and other relevant questions on stem cell biology and organoid development.

Prisca Liberali

What inspired you to become a scientist?

What really drove me was a curiosity to understand how the world around me works. I always had a lot of questions, and I was always fascinated by counting and quantifying the things around me. My secondary school science teacher was a very good teacher and was very important to me. My parents were influential as well, but not directly for science – my mum helped me to be authentic and follow my dreams; my dad was an engineer before he moved into policy making, and he taught me how to build things. I think that helped a lot.

How did you make the decision to go to Italy for your studies?

I was born in Belgium, and I lived between Belgium and Luxembourg because my parents worked for the European Union. I always lived abroad and everybody would ask me 'where do you come from?' and I would say I was Italian but I'd never lived in Italy. So I decided to go to Italy for university and study chemistry. I then had an opportunity to do a PhD in chemistry, but I was always interested in something a bit more complex. Fortunately, I met Daniela Corda who showed me that biology had what I was looking for, so I decided to do a PhD with her [and Alberto Luini].

How was it moving from Belgium to Italy and what memories do you have of that transition period?

It was very hard. One part was related to science – I started my university studies in chemistry and I thought that everybody would be like me, really convinced they wanted to do chemistry since they were 13 years old. Then I arrived there and it was full of people who really didn't like chemistry. I thought that was weird, so that was my first cultural shock. The other issue was the day-to-day life and how different it was in Italy. It took me a bit of time to adapt. I was 2000 km from home and I'd just turned 18 at that time.

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How do you feel you changed and evolved through the years during your scientific career?

I have changed a lot. I'm a physical chemist, I did membrane trafficking in my PhD, I did high-content screening and membrane trafficking and mapping genetic interactions in my postdoc, and now I do organoids and self-organisation. I always like change and accept the risks that come along with it. I follow my curiosity. It's also important to be humble enough to work in a field you don't know, and try to both learn and see what your different background can bring to it.

Has your background helped you to embrace all the interdisciplinary aspects that are now important in cell biology?

In a way I've had that throughout my career. I've really changed from place to place and finishing in Lucas' [Pelkmans, University of Zurich] lab was very important for me because I could really embrace a lot of these different aspects and apply them to quantitative biology. The question you ask is interesting because what is the trait of each science discipline? I think physicists can reduce the problem to a model very well, biologists can embrace the complexities of a problem directly from their studies, and chemists are fundamentally quantitative. As chemists, we are trained to measure everything and to be data driven, rather than model or hypothesis driven, and this is an advantage in 2020 considering the amount of data we currently have. We have a lot of very different,

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Prisca Liberali and her family during sailing holidays in Croatia

very broad and very big datasets. I'm not biased – I look at the data and try to find out what they tell us.

What questions are your lab trying to answer just now?

We are studying fundamental questions of tissue organisation and, as we call it, the 'design principle' of how tissues are organised. We want to understand how thousands of millions of heterogeneous single cells can create very robust properties and functionalities at the tissue level, but also at the molecular scale. The objective is to really understand the molecular mechanism driving cellular behaviour and how this behaviour can drive the formation of the tissue. Some of the questions we are asking, for example, are: in a population of genetically identical cells that are in the same environment, how do you create patterns and break symmetry? How is the heterogeneity emerging in a population and what are the consequences? How can we use this to understand how tissue develops and regenerates?

What model systems are you currently using in the lab?

We use different types of organoids, like intestinal organoids or gastruloids, and we try to understand how they self-organise into higher-level structures. In this system, all structures can grow from one or two single cells and together they form a fully functional tissue. In the lab, we use both mouse and human organoids. With human organoids, we take a more translatable approach in the sense that we try to look at tissue regeneration. We recently showed that organoid formation is driven by a regenerative process, so we are trying to use the human organoids to look into this. We use mouse organoids to look at the molecular mechanism behind it, and also to find out how to generate different types of structures like the gastruloids.

This is an extremely popular and fast-moving field. What influences your line of research?

What drives my research is trying to use these organoids' full potential and understand what they recapitulate, which disease can be modelled with them and what we can learn from a cellular developmental point of view. A lot of nice studies on metabolism have helped me to understand how these cells can evolve different metabolic identities very quickly, and I think the behaviour of cells that transition between these identities is becoming clearer. We have a lot of information on how metabolism works – different cell types and different cellular states can regulate the metabolic outcome depending on the different nutrients and energy levels they have available. It would be interesting to understand how metabolism is affected by the interconnection of different pathways. Metabolism has been isolated for a long time, but now we get to integrate it much more in our system. This will give us a lot of new information, and the organoids provide us with a great system to start looking at these processes.

"Mentoring is something I really love about this job, but I didn't realise how much time it takes to do it well."

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

The first day I arrived at the FMI there were two postdocs and a technician, and after that some PhD students, so very quickly there were four or five of us. One challenge was dealing with the different personalities. You have people who really enjoy speaking with you every day about every experiment, while others need to think about their experiments and then discuss them with you. It's finding a balance. The worst thing to manage is my expectation of myself, what is really realistic, and how to behave differently with staff, PhD students and postdocs. They all need a different level of attention from my side, and I need to have different expectations for the three different groups. Another important thing is to have a relationship with the students based on trust, and to help them find their inner motivation to finish a project; to have the drive to do it. I think in a new lab, where everybody starts at the same time, it's more difficult because you can't learn from people who are at different stages. Mentoring is something I really love about this job, but I didn't realise how much time it takes to do it well.

After having your lab for four years, does it feel like you're in a different phase now?

Yes. I took a lab management course and I was very open with the lab about it. I think it was very useful to discuss what I learned, and now we are at a very good stage where things are managed really well. Also, I have three staff scientists in the lab, so this helps a lot when new people start. The staff scientists are people who I can really trust and rely on. The biggest challenge I have now is transitioning from a junior to a more senior lab. I have more postdocs and there's not this huge age gap now, which is a bit different in terms of management. I also have to make sure that the PhD students don't rely solely on the postdocs and still come to me. I have more travelling, more faculty and community work, reviewing, boards, all these things. It gets harder to find a good balance between them all.

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

One thing is to think about what you would do if you were not afraid. I sometimes think, 'if I was not afraid, what is the most exciting

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thing I would do?' And then I do it. Another piece of advice is to communicate. Having discussions when people first realise things are not going well helps you to tackle problems very early on. Everybody has problems, everybody makes mistakes, and if you communicate about them at an early stage it can stop things from escalating. Also, trusting your own feelings. In this type of management, it's important to realise that if something is not going as you want, it probably isn't going well for the other person. I would also recommend spending a lot of time teaching your people to become the best scientists they can be. Don't do their experiments for them, but instead help them with their time management and teach them how to write. I expect texts and presentations very far in advance, so that there is time to discuss, correct and learn from mistakes.

"Sometimes good ideas need time, and the courage to just try them."

Does this advice come from experience, or was it given to you by your mentors?

The first piece of advice in particular comes from Lucas [Pelkmans]. One thing he would always say was that in your career, you will probably be remembered for a handful of papers, not for every paper that you write. Sometimes good ideas need time, and the courage to just try them. The other advice I got at the FMI was to start presenting my own data fast. This matches my own ethos – I'm very open with my science. I like bioRxiv and I always present unpublished data because I think it will bring back more than it will take away.

Did you have the same attitude to openness when you were a postdoc?

I've always been very open. I think that came from Alberto Luini, but Lucas [Pelkmans] and Daniela [Corda] are the same. Everybody I've worked with has been very open, so I think it's really a part of me. People sometimes say 'maybe you could keep this [data] for yourself', but I prefer to share it. I think it's really paying back. Another thing that has always been important for me is going to meetings. I have applied for meetings that I thought were important for me to attend, even when I wasn't invited. I would go there even if I just had a poster, and I continue to do this. I would approach people directly, saying 'I read your paper, I'm trying to do this in my lab, what do you think?' If I gave a talk, I would go to a person I didn't know, but who could give me feedback, and I'd ask them what they thought, taking all critical advice. Via this, I met very supportive people who have been extremely important for me.

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

One thing that people might not know is that, since starting my lab, I commute 3.5 h every day because I live in Zurich. That means that most of my writing and thinking is done on a train – I can start a thought and finish it without being interrupted. I also think it helps to embrace life's craziness with a good layer of organisation. Everybody has complicated lives, and that makes it interesting. My husband is Dutch, so my kids speak five languages – borderline too many, I would say – but sometimes you just have to run with what life brings you.