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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Melike Lakadamyali

Melike received a bachelor's degree in physics from the University of Texas at Austin and joined the laboratory of Xiaowei Zhuang at Harvard University for her PhD, which was awarded in 2006. She worked as a postdoctoral fellow under Jeff Lichtman at the Center for Brain Science at Harvard University. In 2010, Melike joined the Institute of Photonic Sciences (ICFO) in Barcelona, Spain, as a junior group leader. She was the recipient of an EMBO Young Investigator Award in 2013 and became senior group leader at the ICFO in 2015. Melike is currently an Assistant Professor of Physiology at the Perelman School of Medicine, University of Pennsylvania. Her work focuses on the development and use of imaging techniques to study cytoskeletal transport mechanisms in cells and neurons, as well as the dynamics and mechanisms of the transcription machinery.

Melike Lakadamyali

What inspired you to become a scientist?

In high school I was attracted to physics and mathematics, because it was very appealing to use logic and analytical thinking to solve problems. I majored in physics, without having a career in science in mind or even knowing what exactly to do with a physics degree – I just wanted to do it because I enjoyed it. At the end of my university time, I decided to gain some practical experience by working in a lab and joined the labs of Josef Käs [now University of Leipzig] and Ken Shih [University of Texas]. It was my first exposure to biophysics, using atomic force microscopy to probe cell mechanics, and it didn't begin in a great way – right on my first day I broke a very precious calibration probe!

A difficult first day at the office!

Not a good start, indeed, but my postdoc mentor was very patient and, over time, I learnt how to do measurements. The observation in this project led to the discovery of a mechanosensitive Ca^{2+} signalling pathway in neuronal growth cones. It was so exciting to have observed something for the first time that no-one had ever witnessed before. It was this feeling that inspired me to do a PhD and to pursue a career in science.

> **"It was so exciting to have observed something for the first time that no-one had ever witnessed before."**

What questions are your lab trying to answer just now?

We address how micro-molecular complexes assemble and how this assembly is regulated–spatially and temporally. Individual proteins rarely work alone inside the cell–they have to interact with other proteins and form these micro-molecular machines to carry out a biological function. These interactions are very dynamic and transient, and have to be tightly regulated. We are probing this in two different biological contexts: one of them is intracellular transport. Here, you have molecular motors that have to interact with scaffolding proteins, accessory and adaptor proteins to form complexes on the membrane of vesicles in order to transport vesicles from one place to another. The other context we're looking at is how the transcriptional machinery drives gene activity; in that case you have transcription factors, polymerases and chromatin-modifying enzymes that have to dynamically interact in a transient way and to organise spatially in order to drive gene activity. We are using advanced microscopy methods, like super-resolution microscopy and single-molecule imaging, and we're also taking a quantitative approach to address these questions.

Such an advanced imaging method is stochastic optical reconstruction microscopy (STORM), pioneered by your PhD supervisor Xiaowei Zhuang. Do you think there will be further technological revolutions in imaging, or is now the moment to harvest all the information that STORM and other methods offer?

We never knew that you could break the diffraction limit and that has been quite revolutionary. I think that these methods will continue to evolve and we will continue to push the limits of spatial and temporal resolution and to develop methods that are compatible with 3D imaging. There is quite a lot to be done to improve the methods and to make them more applicable to cell biology. But they're not going to be the next revolution in my opinion–the real revolution will come from applying these methods to cell biology

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Melike with her family, husband Ramon and son Jan

and making new biological discoveries. We now are starting to see examples, so it's really an exciting time.

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

It was challenging to move to a new country [Spain] and to get integrated into a completely new system, to form a new network and establish yourself in a new environment. As said, I was in Xiaowei Zhuang's research group when STORM was discovered. I was in the middle of this revolution–at the right place and right time. When I started my own lab I wanted to use these methods to look at biological questions and I had first-hand experience to be able to build and use the techniques. But, as for every new investigator, recruiting people was particularly challenging. At the beginning, when I was walking around the Institute of Photonic Sciences or at recruitment events, people would confuse me for a PhD student. It was particularly challenging to be taken seriously and to find a balance between being a peer and being a boss, and to motivate and inspire people to work with you.

…"the real revolution will come from applying these [imaging] methods to cell biology and making new biological discoveries."

How are the challenges that you're facing now different?

It's a special time right now because I'm in the middle of my move from Spain back to the US, to the Perelman School of Medicine at the University of Pennsylvania. I'm excited to have this new opportunity and to move from a small institute, which is highly focused, to a big university with more multi-disciplinary research. It's challenging, but I don't necessarily feel like I'm starting from scratch again, simply because I've set up a lab before. Also, I will have some people moving with me to have continuity. But of course it, again, means having to integrate into a new system and a new funding environment. And there will be a transition period until the end of the year, where I will be going back and forth in between two places.

How do you achieve a work/life balance when you're trying to establish yourself as an independent investigator?

This job takes a lot of dedication and I am lucky because I'm married to a scientist, and he understands this challenge. He has been very supportive of my career–when I spent all night in the office, he would bring me dinner and we could still hang out. But there have been a lot of transitions in my life lately–we have a baby boy now and, of course, I'm moving lab. I really want to be present in the life of my son and to be there for him, but I would also like to follow the passion for my career. Once again, I'm trying to figure out how to reach a balance and how to do both things. I have become more efficient since he was born, less of a perfectionist about every single tiny detail of my work.

What's the most important advice that you were given in your career–that you would pass on to someone about to start their own lab?

Both my PhD and postdoc mentors gave a lot of importance to scientific communication. It has helped me a lot in my career: to communicate the results of your experiments, and why they're interesting and relevant to a broader audience. This isn't necessarily something that a lot of people give huge importance to. Public speaking doesn't come natural to me; I still get really nervous before every talk and I, therefore, like to practice. As for my students, for every conference talk they give we always do practice talks and give feedback. I put a lot of importance on this and I try to pass this idea on to the people in my lab.

What is your advice on establishing good collaborations?

When you're doing multidisciplinary work, collaborations are really important. As said before, it helps to give good talks to find productive collaborations because, if people get excited about what you're doing after they hear you present, they talk to you and things evolve from there. For someone who is trained in methods and applying those methods to biological questions, it actually can be quite challenging to strike a balance; you get bombarded sometimes with a lot of enquiries about STORM, for example. You run the risk of spreading yourself too thin if you engage in every project. Collaborations take a lot of dedication–you have to be careful to choose things that are really interesting for you, and also to work with people who you're compatible with and with whom you have complementary expertise.

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

I grew up in Cyprus–my grandparents were farmers and I spent a lot of time with farm animals. I had rabbits and sheep as my pets, and I explored the surrounding forests and crop fields during my childhood. I sometimes think about what it would be like to have such a life. Of course, it was physically exhausting work but, in a way, a simpler lifestyle and I have very fond memories of it. I had a big family and we would all gather around a big table during the holidays and enjoy each other's company. This is becoming harder and harder to do these days with people living in different places all over the world. But I have a soft spot for farm life.

Melike Lakadamyali 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.