Ana-Maria Lennon-Duménil: A dynamic career

Lennon-Duménil uses quantitative biology to investigate the spatiotemporal regulation of antigen presentation.

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Lennon-Duménil under the Chilean sky

Ana-Maria Lennon-Duménil was born in Santiago, Chile, but spent her childhood in France, after her family emigrated when Augusto Pinochet came to power. Her father's sister was a biochemist in France, and it was in her aunt's lab that Lennon-Duménil first caught the science bug. At the early age of eight she decided to become a scientist and never looked back.

Lennon-Duménil was less quick to narrow her scientific focus, perhaps because of what she calls her "compulsive curiosity." Although she now considers her greatest accomplishment the description of an evolutionary mechanism that allows cells to coordinate movement and function, her interests did not always lie in cellular dynamics. She completed her undergraduate studies in biology at the Universidad de Chile after her family returned to the country in 1988. After a PhD fellowship at the Pasteur Institute in the genetics laboratory of Marc Fellous, she conducted postdoctoral studies at Harvard University with the immunologist Hidde Ploegh. Below, she shares how these experiences led to a career investigating the spatiotemporal regulation of antigen presentation.

What interested you about your current area of study?

I am extremely curious and therefore get easily attracted by different disciplines and research areas. I felt fascinated by the process of antigen presentation very early on but had the need to explore it from different perspectives, including genetics and molecular biology during my PhD (studying the transcriptional regulation of MHC class II expression) and biochemistry during my postdoc (studying the proteases involved in antigen presentation). However, the day I felt that I had found what I wanted to focus my career on was the day I did my first time-lapse movie of a cell! Looking at cellular processes in real time just enchanted me.

Then a collaboration with Matthieu Piel, a cell biologist and biophysicist at Institut Curie, and Raphaël Voituriez, a theoretical physicist, taught me to predict cell behavior by looking at these movies in a quantitative manner. I found this very satisfying for various reasons. First, this type of approach attempts to explain biological processes with few essential parameters, which I think generates more robust knowledge than classical biological approaches. Second, it opened my mind to phenomena I had not considered 10 years earlier. For example, cells respond not only to biochemical components but also to mechanical ones, such as the geometry and rigidity of their environment. Finally, quantitative biology reveals how dynamic cellular processes are, which I think is the secret of life. Dynamics allow biological systems to evolve through interaction with their environment.

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What are you currently working on? What is up next for you?

My "niche" has been to use quantitative biology to understand the behavior of B lymphocytes and dendritic cells in light of their antigen presentation function. I am fascinated by cell biological processes such as cytoskeletal transport and membrane trafficking but feel the need to study them in the context of physiology. I find immune cells are ideal for this. Using such an approach, we have unraveled fundamental cell biological mechanisms that allow antigen-presenting cells to coordinate different cellular processes in time and space, including: the coordination of antigen macropinocytosis and cell migration in dendritic cells, which optimizes their environment-patrolling function (1–3); and the coordination of synapse formation and centrosome polarization in B cells, which couples antigen extraction to processing and presentation (4, 5). The dynamics of the membrane-cytoskeleton interface appear to be the main actor in coupling distinct biological processes at the level of the cell.

Several questions were raised by these findings. One is how these molecular mechanisms are regulated by the extracellular cues to which dendritic cells and B cells are exposed in tissues. We are particularly interested in the physical cues like tissue rigidity, geometry and hydraulic pressure, because they are far less studied than the biochemical ones. Macropinocytosis further emerged as a tightly regulated process that might have functions other than antigen capture in dendritic cells, such as linking nutrient uptake to migratory capacity. I think macropinocytosis has been understudied, with many basic questions that remain unanswered. Why do some phagocytic cells perform macropinocytosis

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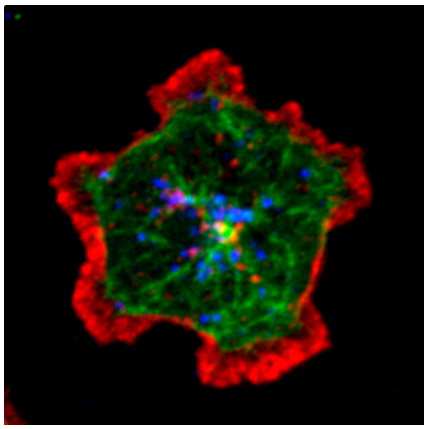

IMAGE COURTESY OF PABLO SAEZ

The B cell immune synapse with actin (red), tubulin (green), and lysosomes (blue).

and others do not? Does this involve the biophysical properties of their plasma membranes? Cancer cells are often macropinocytic. What are the roles played by macropinocytosis in physiology and pathology? We will be putting some energy into answering these questions in a quantitative manner.

What kind of approach do you bring to your work?

Live-imaging and quantitative biology in tissues and, eventually, live organisms are certainly the way to go. In my craziest dream, I would like to image the dynamics of the main intracellular structures (endolysosomes, golgi, ER, nucleus, mitochondria, centrosome, cytoskeletons) while immune cells evolve in their natural environment and perform a specific function. This would bridge molecular, cellular, and tissue scales to reveal how they integrate to optimize immune cell function in an intact organism. I am going to do a sabbatical next year in a zebrafish lab, because I think this animal might be a good model for moving towards this dream.

What has been the biggest challenge in your career so far?

Becoming a group leader and learning to manage a group of human beings that need to be treated differently so that the team works in an optimal collective manner.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader? What were you unprepared for?

I learned to follow my own ideas without being scared of thinking differently, but always in interaction with my scientific environment. I enjoy very much in the Curie Institute that people are open to collaboration. I learned to always try to get the best from the people that surround me, including my PI and colleagues, as well as my students, postdocs, and technicians. I realized that the success of a research group should come from its diversity, so I try to be positive about the different ways of thinking and apprehending science others have. It took me some time and many managing mistakes to realize this, unfortunately!

> "One should enjoy the research process itself more than get obsessed with obtaining results."

What hobbies do you have?

I enjoy meeting different people through theater, books and movies. I like to cook for my family and friends. I usually say that this compensates for the experiments I stopped doing 10 years ago! I enjoy very much interacting with people in general. I love to swim in cold water.

What is the best advice you have been given?

To experience research on an everyday basis, to valorize every small result that makes you move on (or sometimes move back!). One should enjoy the research process itself more than get obsessed with obtaining results, as those come naturally if the process is properly carried out.

Any tips for a successful research career?

Find your own path with no fear of being different. Take the best from the people you work with and enjoy every step!

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The Lennon-Duménil lab in 2015