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First person – Nicola De Franceschi

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Nicola De Franceschi is co-first author on 'ProLIF – quantitative integrin protein–protein interactions and synergistic membrane effects on proteoliposomes' and first author on 'The ESCRT protein CHMP2B acts as a diffusion barrier on reconstituted membrane necks', companion papers published in the 'Reconstituting Cell Biology' special issue in Journal of Cell Science. Nicola conducted the research in the first of these articles while a PhD student in the lab of Johanna Ivaska at Turku Centre for Biotechnology, Turku, Finland. He is now a postdoctoral fellow, and conducted the research in the second article, in Patricia Bassereau's lab at Institut Curie, Paris, France, where his research focuses on *in vitro* reconstitution of ESCRT-III machinery.

Nicola De Franceschi

How would you explain the main findings of your paper in lay terms?

In bottom-up synthetic biology, the basic components that make up a cell, such as lipids, proteins and DNA, can be combined outside of the cell (*in vitro*) and then be used as an alternative way to gain insight into the processes occurring in living organisms.

In the first project (ProLIF – quantitative integrin protein–protein interactions and synergistic membrane effects on proteoliposomes), we designed and purified minimal artificial integrins, which are proteins in the cell membrane that allow the cell to adhere to the surrounding environment. We reconstituted these artificial integrins into model membranes, and developed a sensitive method to quantify the interactions of integrin-binding proteins.

In the second project (The ESCRT protein CHMP2B acts as a diffusion barrier on reconstituted membrane necks), we generated cell membrane structures *in vitro* that resemble dendritic spines, tiny structures that extend out of nerve cells. We tried to understand how proteins move across the base of these artificial 'spines', a process that is important for spine development and plasticity and, ultimately, for nerve cells to be able to communicate with each other. We found that a protein called CHMP2B, which is involved in neurodegenerative diseases, blocks protein movement, thereby potentially regulating nerve cell function.

The common denominator between the two papers is the reconstitution of proteins in an artificial membrane environment that more closely resembles the physiological one. This is an aspect that, owing to technical challenges, is still poorly investigated in synthetic biology.

Were there any specific challenges associated with this project? If so, how did you overcome them?

In the first project, the main (and still unresolved) challenge is to recruit higher-order complexes of cytoplasmic integrin interactors. Although there are certainly technical limitations to the system, my feeling is that we have still not managed to understand some pivotal concepts in how these complexes assemble. A main concept, which is a cornerstone in many biochemical systems but still rarely implemented in synthetic biology, is protein auto-inhibition.

In the second project, the main challenge was technical, namely the manipulation of giant unilamellar vesicles (GUVs) and membrane nanotubes, especially after GUV fusion. Overcoming this obstacle required a lot of practice, but it was nevertheless one of the most fascinating parts of the study. 'Manipulation' is a very appropriate term: our system allows one to touch, move and shape membranes with one's hands, bridging the macroscopic and microscopic worlds.

> **"I realized that I could investigate sequential molecular events occurring on a membrane geometry that had previously been inaccessible for CHMP proteins."**

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

In the second project, I had been testing a number of established methods for obtaining membrane fusion, but they all required

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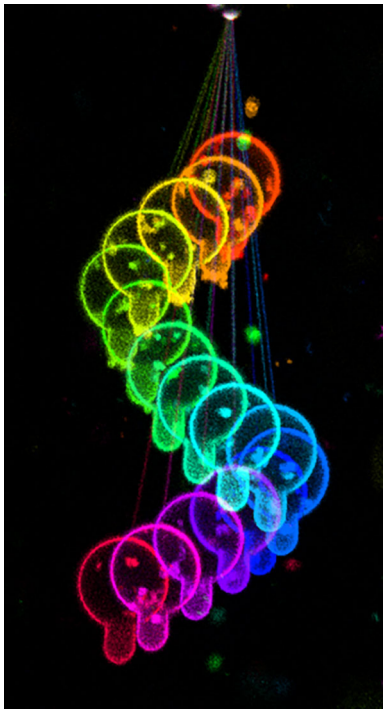

Temporal color-coded movie of a GUV dangling from a membrane nanotube.

extreme experimental conditions that were incompatible with proteins as capricious as CHMPs. When I obtained the first fusion events using laser-mediated heating of gold nanoparticles, and when I saw that the pre-existing nanotube could withstand the fusion event, I realized that I could investigate sequential molecular events occurring on a membrane geometry that had previously been inaccessible for CHMP proteins.

Why did you choose Journal of Cell Science for your paper?

Journal of Cell Science has an excellent reputation. Once I discovered that there would be a special issue on synthetic biology, I felt it was a natural choice. Bottom-up synthetic biology has huge potential, but scientists working in its different branches need to be brought together to integrate their knowledge and work more closely with cell biologists. I believe that Journal of Cell Science and particularly the issue focusing on 'reconstituting cell biology' is a perfect setting and a timely opportunity to do exactly that.

Have you had any significant mentors who have helped you beyond supervision in the lab?

I am very grateful to my PhD supervisor Johanna Ivaska, who has largely exceeded her duties, providing guidance and precious advice well after my PhD was over. What I treasure most is the enthusiasm and positive attitude that she was able to instill in me, which is ultimately the mind-set that makes science worth doing. I would also like to thank Patricia Bassereau for giving me the opportunity to work with reconstituted membrane systems and gain this important expertise.

"Be stubborn when needed, but also learn when it's best to drop an unsuccessful idea; it keeps you from wasting precious time."

What's the most important piece of advice you would give to a first-year PhD student?

Choose the right question to pursue. It will be your focus for the next three to four years, so let it be worth your time and effort, and choose something that keeps you curious and engaged in spite of the ups and downs. Be stubborn when needed, but also learn when it's best to drop an unsuccessful idea; it keeps you from wasting precious time.

What changes do you think could improve the professional lives of scientists?

The list could be very long, but something that could definitely save scientists' time and resources, and greatly improve science credibility, is to give more credit to studies that are actually reproduced.

What's next for you?

I am expecting important breakthroughs in the field of bottom-up synthetic biology in the next few years. Approaches that have been developed separately, such as microfluidics, DNA origami, *in vitro* translation and transmembrane protein reconstitution, just to mention a few, are being combined in creating more and more complex systems. I would like to become an independent scientist in this field and make my contribution to this exciting endeavor.

Tell us something interesting about yourself that wouldn't be on your CV

I love art in its various forms, and I think this passion contributes to shape my mind-set about science. I tend to regard science, at least some of it, as a kind of artistic expression, and I believe that the possibility of combining science with art could make it more entertaining and, importantly, accessible to the general public.

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