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FIRST PERSON

First person – Francesco Consolato

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. Francesco Consolato is joint first author on 'm-AAA and i-AAA complexes coordinate to regulate OMA1, the stress-activated supervisor of mitochondrial dynamics', published in Journal of Cell Science. Francesco is a postdoc in the lab of Giorgio Casari at San Raffaele Scientific Institute, Italy, investigating basic cell biology such as the interaction and regulation of metallopeptidase and their substrates.

Francesco Consolato

How would you explain the main findings of your paper to non-scientific family and friends?

The human organism is composed of billions of cells, each of which needs energy to perform its specific work. This energy is produced by special factories named mitochondria, with each single cell containing a high number of these 'power houses'. To maintain high standards of energy production, mitochondria continuously fuse with other mitochondria or fragment themselves into smaller parts to isolate the broken machines of the factory. This mechanism is called mitochondrial dynamics, and specific sentinel proteins finely regulate these unceasing movements. One of the most important is a protein named OMA1, whose work is fundamental to the fragmentation of altered mitochondria. In our work, we identify a mechanism that involves two other mitochondrial proteins, AFG3L2 and YME1L1, which are able to regulate the amount of OMA1. These findings demonstrate that there is a fine system of balance within cells that protects the production of energy in mitochondria.

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

In this project, one of the most challenging moments was to demonstrate the physical interaction between OMA1 and AFG3L2, since the kinetics of a protease and its substrate is too fast to be detected with a co-immunoprecipitation experiment. To stabilize this reaction, we used a proteolytically inactive mutant of AFG3L2, which is able to interact with its substrates but is not able to process them. With this adaptation, we were able to decrease the reaction velocity and detect the physical interaction.

"Remember that in these three years the most important thing that you have to do is to change your way of thinking"

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

In this work there were two 'eureka' moments. The first one was when we observed that overexpression of wild-type AFG3L2, but not the proteolytically inactive mutant, was able to recover OMA1 processing in *Afg3l2* knockout cells, providing *in vitro* evidence of the accuracy of our model. The second and most important 'eureka' moment was when we were able to detect endogenous OMA1 protein, in addition to the tagged form, with a new antibody. Thanks to this antibody, we could confirm the results previously obtained in overexpression conditions.

Have you had any significant mentors, and how have they helped you?

I have had two significant mentors that helped me; the first one is Prof Giorgio Casari, and the second, but no less important, is my PhD supervisor Francesca Maltecca. Both of them taught me valuable lessons that I'll always keep in mind and continue to share with younger lab-mates. Professor Casari taught me that in science, nothing can be taken for granted and, in particular, that if you are the youngest, to take what other people say with a major grain of salt and to always check for yourself. By contrast, Francesca supervised me every single day, teaching me the scientific method. She explained to me the importance of having the right controls in every experiment and the importance of being the first and harshest reviewer of my own work.

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

The most important advice I could give first-year PhD students is to always keep in mind what PhD means. In the title of Doctor of

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Philosophy, the most important part is the word 'philosophy'. This word derives from the ancient Greek *philosophia* and could be translated as 'love of wisdom'. You must be curious, you must always ask yourself "Why?", "How do these processes work?" and "Is there some experiment already described in the literature that can help me understand?".

Before starting an experiment, spend some time studying the literature; don't discard old papers just because they don't look very pretty. You should go to your bench only when you know all the variables and when you have in mind all the possible results. Remember that in these three (at least) years, the most important thing that you have to do is to change your way of thinking. Up until now someone has provided the answers to your questions, but from this moment on you are the only person that can provide the answer!

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

I think that there are at least three changes that could improve the professional lives of young scientists. The first one is related to funding. Every institute could create a dedicated fund by applying a sort of 'tax' on the bigger grants, which could then be redistributed to deserving young scientists. The second change is related to university early-career scientists who are obliged to spend many hours giving lectures, subtracting a huge amount of time from their research at a point in their careers where study and bench work should be the priority. The third change is related to the public perception of PhD courses and research in Italy. Often, research is not considered as 'real' work, but is seen as a sort of hobby; from a legal point of view, it is not regulated in the same way as other jobs. This causes a lot of complications in a researcher's daily life. To resolve this issue, we will need a profound cultural change.

What's next for you?

In the next few years I would like to continue my research activity in the cell biology field. I love investigating unknown mechanisms and trying to clarify them but, in the meantime, I also love the possibility of creating new tools that could be useful to other scientists for cell biology studies or for medical diagnosis. That's something that deeply stimulates my brain.

Reference

Consolato, F., Maltecca, F., Tulli, S., Sambri, I. and Casari, G. (2018). m-AAA and i-AAA complexes coordinate to regulate OMA1, the stress-activated supervisor of mitochondrial dynamics. *J. Cell Sci.* **131**, jcs213546.