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FIRST PERSON

First person – Pablo Sánchez and Franziska Kriegenburg

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Pablo Sánchez and Franziska Kriegenburg are co-first authors on 'ULK1-mediated phosphorylation regulates the conserved role of YKT6 in autophagy', published in JCS. Pablo is a postdoc in the lab of Claudine Kraft at Institute of Biochemistry and Molecular Biology, Faculty of Medicine, University of Freiburg, Germany, investigating the molecular mechanisms regulating autophagy in different organisms. Franziska is a postdoc in the same lab working on understanding the regulation of protein degradation pathways and the impact on cellular fate.

Pablo Sánchez

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

P.S. and F.K.: When cells need to degrade components, they have a waste disposal system called autophagy. Similar to what happens in our cities, the unwanted materials are collected in a specific vehicle, a membranous compartment called autophagosome, which then delivers it to the recycling station of the cell. Like any complex system, this needs fine-tuned regulation. One of the key steps is deciding when the waste is allowed to enter the recycling station. In our paper, we found that ULK1, one of the early regulators of this recycling process in mammals, is also responsible for the regulation of the final step through a protein called YKT6. Furthermore, we also found that this regulation is conserved from yeast to worms and mammalian cells. This indicates that not only the main biological processes, but also many steps of their regulation, are conserved between distant organisms.

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

P.S. and F.K.: One would think that trying to see how a process is conserved in different organisms would be an easy task, as you think you know what you are looking for. Still, there are many differences between yeast, mammalian cells and worms, and although the key steps of the process were conserved, there were many challenges working with the different organisms. This highlights that collaborations with other teams are key in science, as no lab can be expert on everything.

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

P.S. and F.K.: Fluorescence microscopy was a big part of this project, but the fact that YKT6 is mainly a cytosolic protein made it almost impossible to visualize its association with membranes, which was a key point we had to assess. We had to optimize a method to permeabilize the plasma membrane in live cells to remove all the soluble background, but once we figured it out, we could clearly see YKT6 on membranes! Half of our microscopy experiments rely on this permeabilization, so we are very happy that it worked so well. An example of this method can also be found in the accompanying figure.

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

P.S. and F.K.: We had published in the journal before and were very happy with how the process went. Also, JCS is known for great publications in the autophagy field.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

P.S. and F.K.: We had no special guidance on this project besides supporting ourselves in the team, but we were given advise by several experts in the autophagy field. We are thankful for the nice international community working on this topic.

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

P.S. and F.K.: Curiosity is probably the most motivating aspect. Another important aspect is the science community, which we mainly experienced as supportive and compassionate – very much family-like. Going to meetings and conferences and seeing the outcome of the work from other groups is extremely motivating, and the exchange can sometimes help you decide which direction to pursue; this makes smaller conferences

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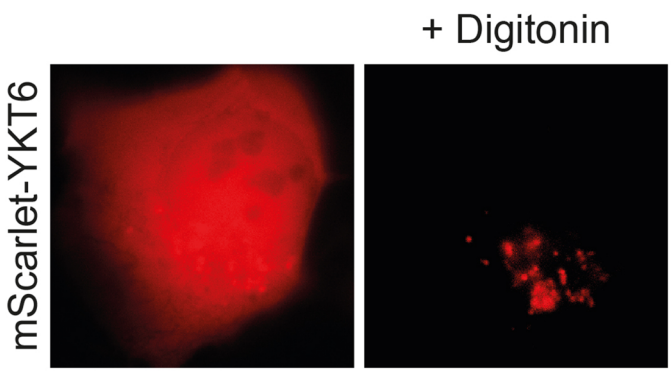
Franziska Kriegenburg

in particular some of the most interesting moments during our careers. Also, it shows that you do not struggle alone, which is somehow relieving.

Who are your role models in science? Why?

P.S.: Science sometimes feels like a niche job, where you do things so specific that only a few hundred people in the world would understand or care about your efforts. In that sense, I admire scientists like my first mentor, Carlos Romá-Mateo, who take upon themselves the challenge of making science understandable for the broad public. This should always be a priority for publicly funded research and I find it very sad that sometimes it seems detrimental for your academic career to do anything that is not your own research.

F.K.: In each state of my career, I have met people who have left a deep impression. My early supervisors during my studies and PhD, especially Klavs B. Hendil and Rasmus Hartmann-Petersen, were always cheerful and taught me that a failed experiment or broken column is not the end of the world, and that part of sincere science is staying upbeat with a healthy distance. Something that is much easier when having awesome, smart and supporting lab members,



Digitonin permeabilization allows the visualization of membrane-associated proteins. Live-cell imaging of a HEK293 cell expressing mScarlet-YKT6. After 15 min permeabilization with digitonin, cytosolic mScarlet-YKT6 has been washed away from the cell and membrane-bound YKT6 becomes visible.

such as Pauline Verlhac, Idil Orhon and Mariya Licheva, to name only a few. Importantly, one should reflect how one's own behavior impacts other people.

What's next for you?

P.S. and F.K.: Project-wise, now that we have confirmed that the role of YKT6 is conserved among organisms, it would be very interesting to dissect why some organisms have more than one SNARE protein on the surface of the autophagosome while others rely only on YKT6. Are they redundant, or is this a way to distinguish between autophagosomes with different sizes and cargos?

P.S.: Career-wise, I will likely pursue a career outside academia. I really enjoy coordinating and discussing (research) projects and feel that I will have more options at this career stage in the private sector.

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

P.S.: I have done many courses on leadership and management, but in the end, I have found that the key for a good relationship with your colleagues is to have a well-supplied drawer full of snacks in your office. People will come to discuss science with you way more often if you have their favorite cookies at hand.

F.K.: I believe that labs and companies could be run more eco-friendly and that there are several ways to reduce the plastic waste accumulating in a research lab. So, I always encourage my colleagues to reflect on their plastic consumption, e.g. rather use re-usable material like glassware when possible or wash certain types of plastic.

Reference

Sánchez-Martín, P., Kriegenburg, F., Alves, L., Adam, J., Elsaesser, J., Babic, R., Mancilla, H., Licheva, M., Tascher, G., Münch, C. et al. (2023). ULK1-mediated phosphorylation regulates the conserved role of YKT6 in autophagy. *J. Cell Sci.* **136**, jcs260546. doi:10.1242/jcs.260546