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FIRST PERSON

# First person – Eric Clement Arakel

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. Eric Clement Arakel is first author on 'Dissection of GTPase-activating proteins reveals functional asymmetry in the COPI coat of budding yeast', published in JCS. Eric Clement is a post-doctoral research associate in the lab of Blanche Schwappach at Universitätsmedizin Göttingen, Department of Molecular Biology, Göttingen, Germany, investigating the use of structure-guided manipulations of the COPI coat to dissect the molecular mechanisms that mediate the ER-retrieval of proteins from the Golgi.

Eric Clement Arakel

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

Spherical carriers called vesicles transport proteins and lipids from one part of the cell to the other. Vesicle coats, much like a cage around these spherical carriers, decide what to pack into these vesicles. Molecular coats are diverse and are restricted to specific locales within the cell. These coats sculpt the forming vesicle as it outgrows from the donor membrane. Once released into the cytoplasm, lasso-like proteins help to tether and guide the vesicles to the right target site. The vesicles then empty their contents by fusing with the appropriate site. Vesicle uncoating, a process where a vesicle sheds its enveloping coat, is a prerequisite to vesicle fusion.

Our paper dissects two proteins called ArfGAPs, which help dismantle the COPI coat, a coat that typically retrieves proteins and lipids from the Golgi to the endoplasmic reticulum. In this paper, we demonstrate that the two COPI-associated ArfGAPs in yeast, Gcs1 (the homolog of mammalian ArfGAP1) and Glo3 (the homolog of ArfGAP2/3), although believed to be functionally similar, are in fact quite distinct. We draw out the differences between the two ArfGAPs and also demonstrate that the process of COPI vesicle formation is highly regulated.

**"…Gcs1 (ArfGAP1) and Glo3 (ArfGAP2/3), although believed to be functionally similar, are in fact quite distinct."**

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

The roles of the COPI-associated ArfGAPs have been discussed and debated at length by several labs. Distinguishing whether the two ArfGAPs (three in mammals) serve specific roles in the COPI coat has always been a tricky point in question. By using catalytically inactive mutations of the two yeast ArfGAPs, coupled with insights from recent structural work on the COPI coat, we demonstrate that the two ArfGAPs occupy distinct niches within the coat and that they perform specific functions in the COPI lifecycle, besides their canonical role in stimulating GTP-hydrolysis in Arf GTPases. This structure-guided approach helped to draw our attention to a key regulatory element in Glo3 (ArfGAP2/3) that possibly helps to stabilise the COPI coat on membranes.

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

The stark difference in cell viability following the expression of catalytically inactive Gsc1 (ArfGAP1) or Glo3 (ArfGAP2/3) was definitely a moment of revelation. We were equally amazed by the discovery that this outcome could be tracked back to an evolutionarily conserved stretch, and that this element was regulated by phosphorylation, possibly serving as a timer during coat assembly.

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

We published a review titled 'Formation of COPI-coated vesicles at a glance' in the Journal of Cell Science early last year. In this Review, we discussed decades of research on COPI in the context of current structural models and highlighted several significant yet unresolved questions in the field. The uncertainty regarding the precise roles and orchestration of ArfGAP stimulated GTP-hydrolysis in Arf was one of the themes that featured prominently in our Review. Given that the Review helped us focus our attention and fine-tune the experiments described in this paper, we decided that Journal of Cell Science, catering to a large audience of

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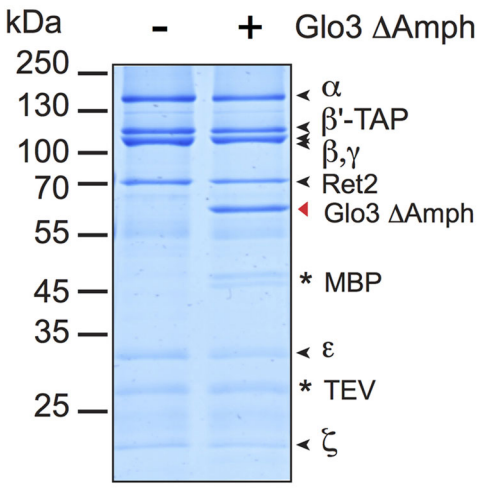


***In vitro* reconstitution of a stoichiometric COPI-Glo3 complex.**

fellow cell biologists, was the perfect platform to have our work publicised.

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

I am fortunate to have had Blanche Schwappach as my mentor. I have learned a lot from her standards on rigorous experimentation, her organised workflow, her willingness to share scientific discoveries and foster collaborations, her tactful diplomacy and her constructive appraisal of work from fellow researchers. Over the years, I have also collaborated with several amazing scientists and they have all helped shape me into the person I am today. The list is long. You all know who you are!

**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?**

I have always been fascinated by how things work, so a career in science seemed quite obvious to me. I have loved exploring how complex cellular machines, such as ion channels and vesicle coats, are assembled and how they scrupulously effect their roles within the cell. Through several collaborative ventures, I have got to meet many interesting people across the globe and have found the constant exchange of ideas and endless learning intensely refreshing. The euphoria of scientific discovery has also often been a heady stimulant. Looking back, I quite don't think I would do anything differently.

**Who are your role models in science? Why?**

I've had several role models in science, mostly people whom I have known and worked with. I hold them in high regard for several reasons: scientific rigour and integrity, clever out-of-the box thinking, accurate and creative communication of their work, the virtue of patience and mutual respect, being able to handle the inevitable experimental slumps with a level head, and maintaining a great work–life balance. Truth be told, role models are rarely the full package! You simply have to draw on their most inspirational qualities, piece them together and hope to shape a better version of you.

## "Truth be told, role models are rarely the full package!"

**What's next for you?**

After several years of research in academia, the lines between my hobby and my career have become blurred. This does have its fair share of pros and cons. However, being someone who likes to shake things up and learn something new, I have recently decided to leave academia and research. It has been difficult for me to walk away given my passion for scientific research and the relative flexibility it affords. However, after much self-contemplation, I have decided to make the leap. September this year ushers in a new and exciting beginning, and I am delighted to have this body of work published in the Journal of Cell Science, perfectly in time, on my way out.

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

I love gardening. I did try my hand at bonsai a long time back, but realised it was a rather expensive hobby, and one that required more commitment than I could invest at the time. I hope to revisit crafting bonsai and perhaps take up angling someday.

**Reference**

**Arakel, E. C., Huranova, M., Estrada, A. F., Rau, E.-M., Spang, A. and Schwappach, B.** (2019). Dissection of GTPase-activating proteins reveals functional asymmetry in the COPI coat of budding yeast. *J. Cell Sci.* **132**, jcs232124. doi:10.1242/jcs.232124

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