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FIRST PERSON

First person – Mathias Cobbaut and Ahmed Elbediwy

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. Mathias Cobbaut and Ahmed Elbediwy are co-first authors on 'The Rho family GEF FARP2 is activated by aPKCι to control tight junction formation and polarity', published in JCS. Mathias is a postdoc in the lab of Prof. Peter Parker at The Francis Crick Institute, London, investigating protein kinase regulation/biochemistry and the functional role of protein kinase signaling. Ahmed is a lecturer at Kingston University, investigating cancer biology, polarity and signaling.

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

MC and AE: For cells to develop into functional tissues, they need to be correctly positioned. In epithelial tissues, individual cells need to know their 'top' and their 'bottom', because these two sides of the cell have unique properties and this is known as cell polarity. If you think of a magnet, for instance, it has two poles, and a cell is very similar. In this article, we identified a role for the protein FARP2 in cell polarization. Specifically, we found that FARP2 acts as an activator for Cdc42, a protein that is essential for polarity. Cdc42 works with another protein called aPKC to establish cellular polarization and to allow cells to stick to each other in a process called cell–cell adhesion. We found that aPKC modifies FARP2, which seems to drive its correct localization and complex turnover at cell–cell junctions to establish junction formation and maintenance.

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

MC and AE: The challenges in this project were on the mechanistic level. Initially, we hypothesized that aPKC-mediated phosphorylation of FARP2 would modulate its activity to increase active Cdc42 levels in a positive-feedback-loop mechanism. That would have been a straightforward answer and matched the observed phenotype seen with non-phosphorylatable mutants of FARP2. However, the picture seemed to be more complicated. FARP2 phosphorylation did not affect the overall levels of active Cdc42; rather, we found that phosphorylation mediates correct localization of FARP2 to the tight junction compartment and enhances aPKC–FARP2 complex turnover in order to liberate FARP2 to activate local pools of Cdc42. Untangling this mechanism was quite the challenge in this project, but we do like these mechanistic puzzles, so in the end, it was quite rewarding to solve it!

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

MC: I would say that the eureka moment within this project was when we uncovered the mechanistic consequence of FARP2 phosphorylation and put the pieces of the puzzle together to draft an optimized model.

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Mathias Cobbaut

AE: I also think another eureka moment was earlier in the project when we observed how effective the FARP2 phenotype was in comparison to FARP1.

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

AE: As one of the leading cell biology journals, it was clear that we wanted our novel research to be published in JCS. With over 150 years of experience in publishing groundbreaking papers, it was the obvious choice.

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

MC: I would like to mention Peter Parker's mentorship, since his constant support and his ideas for different hypotheses helped to shape this paper (but also my work in general). My joint first co-author Ahmed has also been a great example to me in this process. Ahmed would never let his drive and enthusiasm diminish. He is like a pitbull biting a bone; once something is of value to him, he will not release it, which is an inspiring attitude, I have to say. In a more general sense, I have to mention my PhD supervisor and co-supervisor, Johan Van Lint and Veerle Janssens at the KU Leuven (Belgium), who have been very supportive of me, not only with regards to career choices and establishing connections, but also in exposing me to the wider cell signaling field, helping me to understand the 'people factor' in science, and channeling my enthusiasm towards good research. Finally, the general mentoring environment of the Francis Crick Institute is very inspiring. The institute has been built to nurture informal scientific discussion with

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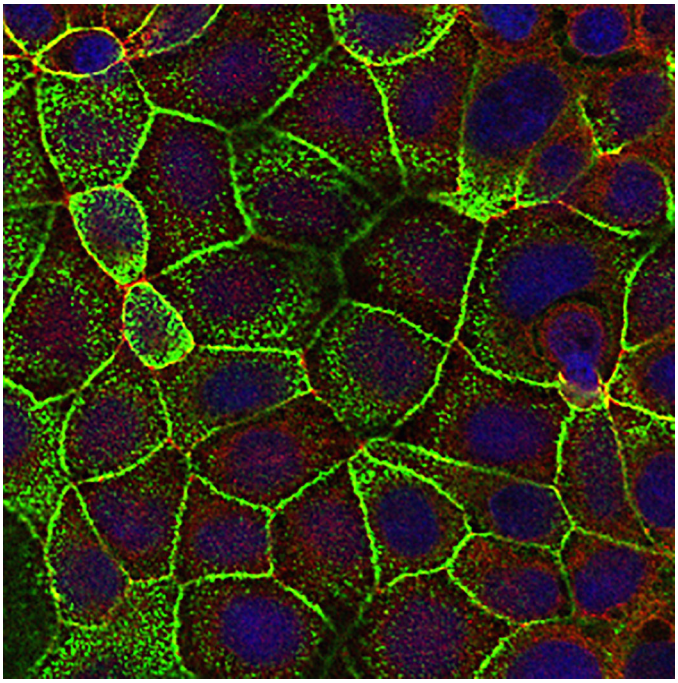
a variety of inspirational people that are on top of their game, studying versatile research topics. It is hard not to be swept up by the energy that radiates out of this building!

AE: I would also like to give credit to Peter Parker for allowing me to collaborate with his lab on this amazing project. The other person I wish to mention is of course my joint first co-author Mathias.



Staining of apical cell polarity proteins that provide a scaffolding function for various signaling molecules.

He has recently started as a postdoc and his tenacity and resilience are outstanding. He would be working late into the night, as well as over the weekend, having dinner at his desk just to make sure the experiment he is performing is perfect. He has a bright future ahead.

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?

MC: I have always been fascinated by the degree of complexity in the world that surrounds us, but the decision to pursue science as a career was mainly inspired by my high school biology classes around the age of sixteen, where I first came into in-depth contact with molecular biology and biochemistry. I was fascinated by the elegant chemical mechanisms by which life is organized and how even subtle defects in the system could lead to disease. On top of that, we had a very inspirational teacher, which I feel is crucially important for pupils in choosing a STEM career! I am happy with my scientific path to date, especially the support I have had from people along the way. It has been a very interesting, challenging and rewarding period. Some of the interesting moments along the way I would say are: the excitement about the first discovery of something new and 'weird' that has driven me since; my first conference in the field, where I was able to meet all the 'rock stars' I had been reading and hearing so much about; the first paper we successfully published; and the first time I went abroad for a placement. It has all been valuable and has nurtured me to the point where I am now.

AE: The idea of trying to answer a question and investigating the problem is what made me want to do research. There have been many interesting things along the way. One Sunday early in my PhD, I needed some buffer, and my supervisor bought a 20 litre box-style bottle which was on its side – the idea being to unscrew the top and screw on the tap. I tried this while the box was on its side; 20 litres later, I walked – soaked and dripping – to the toilet to dry myself using the hand dryer.

"Research is like a marathon, you will find a few bumps on the way, but if you persevere you will succeed."

Who are your role models in science? Why?

MC: At heart, I'm a kinase biochemist, so I look up to the godfathers and mothers in the kinase field. Examples include Susan Taylor, who crystallized the first kinase (PKA) and has since done a tremendous and relentless job to uncover every detail of its mechanism of action, and Tony Hunter, the discoverer of crucially important Tyr and, recently, His phosphorylation. Both of them were very approachable and supportive when I had the opportunity to meet them. Also chemical biologists, such Jason Chin, whose innovative work blew me away once in a keynote lecture, and Kevan Shokat, whose innovations have been crucial to the kinase chemical genetics field. Both are very inspirational. In general, I look up to scientists who are excited by solid scientific discoveries, even if they are discomforting to their own work. I can also safely say that Peter Parker has been a role model for me, not only for his seminal scientific work in the PKC field but also regarding his management style, which leaves a lot of breathing room for his people to pursue their personal interests within projects and keep their motivation levels high.

What's next for you?

MC: I am at the beginning of my first postdoc so there are many future possibilities depending on my achievements and the contacts that I will establish.

AE: I am currently a lecturer at Kingston University, so I am starting to build my research group and hopefully I will be able to carry forward my research interests on polarity and signaling.

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

MC: As a proud Belgian, I have a keen interest in brewing and subsequently sampling beer.

AE: I'm a proud Liverpool and Egypt national team supporter. Football is a great way to relax after a hard day of research. I also have two football-mad kids who keep me busy!

What advice would you give to a scientist starting out on the path of research?

AE: Research is like a marathon, you will find a few bumps on the way, but if you persevere you will succeed. There will be days where things don't work and you feel like giving up, but keep going and the clouds will lift and the sun will shine.

MC: Never lose your curiosity and sense of amazement.

Reference

Elbediwy, A., Zhang, Y., Cobbaut, M., Riou, P., Tan, R. S., Roberts, S. K., Tynan, C., George, R., Kjaer, S., Martin-Fernandez, M. L. et al. (2019). The Rho family GEF FARP2 is activated by aPKCι to control tight junction formation and polarity. *J. Cell. Sci.* **132**, jcs223743. doi:10.1242/jcs.223743