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FIRST PERSON

First person – Thibault Legal

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. Thibault Legal is first author on 'The C-terminal helix of BubR1 is essential for CENP-E-dependent chromosome alignment', published in JCS. Thibault is a PhD student in the lab of Julie Welburn at the Wellcome Trust Centre for Cell Biology, University of Edinburgh, Edinburgh, UK, investigating kinetochore–microtubule attachment in mitosis.

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

During cell division, all the chromosomes are moved to the middle of the cell where they align before being segregated to each pole. Microtubules are filaments that help align some chromosomes; however, not all chromosomes manage to reach the middle. For those that are misaligned, the presence of a protein called CENP-E is essential. CENP-E is a molecular motor; it can walk on a microtubule and transport a chromosome to the middle of the cell. CENP-E is recruited to a protein scaffold called the kinetochore, which links the chromosomes to the microtubules. How CENP-E is recruited to kinetochores is still unclear. In this paper, we show that CENP-E binds to another kinetochore protein called BubR1, and we determine precisely which part of CENP-E binds to which part of BubR1. We then test the importance of this interaction and show that cells deficient for it have more misaligned chromosomes.

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

As this paper focuses on an interaction between two proteins, I tried hard to obtain the structures of these proteins, either together or independently, without success. A structure would have helped us map more precisely the amino acids involved in the interaction. Instead, I looked at conserved residues in the sequence and turned to low-resolution structural techniques to characterize these proteins. I then made a number of mutations until I could disrupt the interaction.

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

The kinetochore-targeting domain of CENP-E is not well conserved. This made it difficult to identify regions that are crucial for its function. When I carried out an alignment of this domain with species that were more closely related to humans, some conserved regions stood out. After careful analysis, I found four residues that were very well conserved and I hypothesized they would be important for the interaction with BubR1. When I mutated them, I was pleased to see that the interaction was disrupted both *in vitro* and *in vivo*.

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Thibault Legal

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

Journal of Cell Science publishes a lot of studies related to mitosis that I enjoy reading. We thought our study would fit well with the scope of this journal and interest the readers. I have also seen Journal of Cell Science and some of the editors at conferences, which makes it a more approachable journal.

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

My PhD supervisor, Julie Welburn, has been an amazing mentor. She has taught me how to become an independent researcher and gave me the freedom to test my own hypotheses. She has also been very supportive during my PhD, and I am grateful to have her as a supervisor. The other members of my thesis committee, Kevin Hardwick and Ken Sawin, have also been very helpful. They have given me very good advice during my PhD.

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 thought human bodies were really interesting and wondered how everything works. At university, I became interested in cell biology and I realized that there were a lot of unknowns in what we were learning at lectures. The main reason I decided to work in research is curiosity, I could spend my time trying to understand these gaps in our knowledge.

The most interesting moments were when I presented my research at conferences. It is always exciting to see what discussions arise with people who are interested in what you do.

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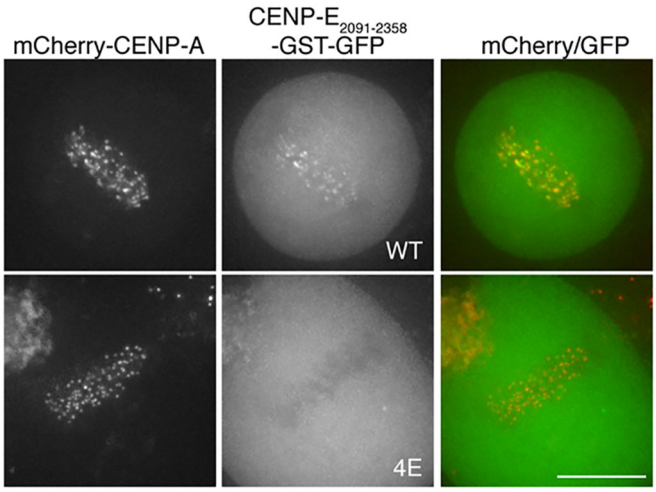

Cells transfected with the domain of CENP-E that binds BubR1, fused to a GFP tag (green). The wild-type construct (top) goes to kinetochores because it colocalizes with CENP-A, which is fused to an mCherry tag (red). When CENP-E has four amino acids mutated so that it does not bind to BubR1, it does not localize to kinetochores anymore (bottom).

“It is always exciting to see what discussions arise with people who are interested in what you do.”

Who are your role models in science? Why?

All the people working to improve LGBTQ+ visibility in science, technology, engineering and mathematics (STEM) and, more generally, everyone supporting and showcasing minorities in STEM.

What’s next for you?

I am planning to graduate next year, so I am currently looking for a postdoctoral position. I really enjoy biochemistry and structural biology, so I would like to keep these aspects in my future project.

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

I love dancing in clubs, especially to techno music. Since all the clubs closed at the beginning of the lockdown, I bought a DJ controller and started DJing to make my flatmates dance. I have had a lot of fun doing it, so I think I will keep this as a hobby.

Reference

Legal, T., Hayward, D., Gluszek-Kustusz, A., Blackburn, E. A., Spanos, C., Rappsilber, J., Gruneberg, U. and Welburn, J. P. I. (2020). The C-terminal helix of BubR1 is essential for CENP-E-dependent chromosome alignment. *J. Cell. Sci.* **133**, jcs246025. doi:10.1242/jcs.246025