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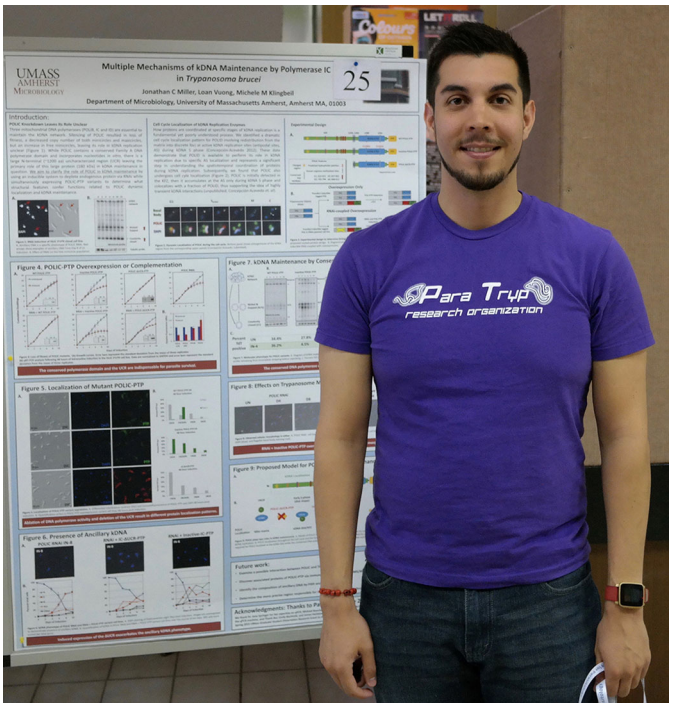
FIRST PERSON

First person – Jonathan Miller

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. Jonathan Miller is first author on 'A DNA polymerization-independent role for mitochondrial DNA polymerase I-like protein C in African trypanosomes', published in JCS. Jonathan is a PhD student in the lab of Dr Michele Klingbeil at the Department of Microbiology, N269 Life Sciences Laboratory, Amherst, MA, USA, investigating mitochondrial DNA replication and maintenance in the eukaryotic parasite *Trypanosoma brucei*.



Jonathan Miller

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

Everyone remembers mitochondria as the 'powerhouse' of the cell and most (hopefully!) remember that these organelles even contain their own DNA. How mitochondria have evolved over time has created fascinating relationships between mitochondria and host, especially for eukaryotic parasites, which undergo dramatic environmental changes in their life cycle. The single-celled parasite *Trypanosoma brucei* causes life-threatening disease in humans and other mammals and, interestingly, each cell contains a single mitochondrion, which provides researchers (like me) with a tractable system to observe mitochondrial biology. In humans, a full complement of mitochondrial DNA are hundreds of circular molecules, and how they are replicated is well understood. DNA in the single mitochondrion of *T. brucei* is made of thousands of DNA rings, all interlocked together, reminiscent of medieval chain mail. Replication and accurate partitioning of all this DNA is a complicated process, and involves enzymes called DNA polymerases that are responsible for creating new DNA off the original template. Our paper describes the unusual role for a DNA polymerase that is involved – not just in a replicative aspect but, also, in appropriate distribution of the mitochondrial DNA.

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

The most challenging aspect with this project was the unexpected multitude of phenotypes to track in either the kDNA status (including intactness, size and localization) or our tagged protein's status (size and number of structures), relative to the cell cycle stage. It was an iterative process of analyzing the images and discussing additional important phenotypes to track. To do this manually in a statistically significant fashion meant countless hours on the fluorescence microscope!

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

The most striking memory is most likely the moment I sat in the dark room and slotted onto the microscope stage a slide of fixed IC-DEAD cells. After the mercury lamp had warmed up and I set the filter to FITC, the tagged mutant fluorescence lit up in a way I had never seen before: the protein appeared to be stuck onto the mitochondrial DNA wholly, regardless of cell cycle stage, in every cell! Because we knew from previous work that protein localization changes based on cell cycle stage, it was incredibly unexpected and mesmerizing to see it light up in that fashion.

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

We wanted to publish in the Journal of Cell Science because of its broad scientific audience and the rigorous approach to publishing high quality data.

"Remember… the most important tool… is the ice bucket!"

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

The mentorship I received by Dr Spencer Nyholm and my then-student mentor Dr Andrew Collins as an undergraduate at the University of Connecticut provided the stepping stones to examine the curious world of microorganisms. Drs Margaret Rubega and Michael Lynes revealed to me the power of effective teaching with innovative test-taking methods and with nothing but a single piece of chalk, respectively. Once at the graduate school at the University of Massachusetts Amherst, my PI Dr Michele Klingbeil put me through 'biochemistry bootcamp', and since then I've never looked back on fascinating and rigorous hypothesis testing. Remember… the most important tool… is the ice bucket!

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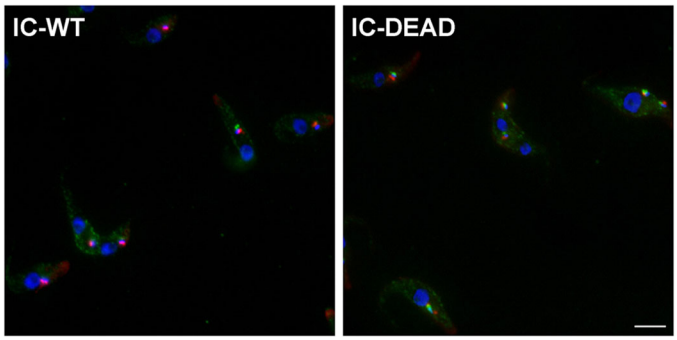

Merged immunofluorescence image of tagged POLIC variants (green), flagellar basal body as cell cycle marker (red) and DNA (blue) stained with DAPI in a field of unsynchronized fixed cells. Scale bar: 5 µm.

What's next for you?

While I am in the writing and conclusion phase of my PhD, I am currently working as a scientist in the biopharmaceutical industry. I was lucky to have been accepted as a co-op student and was subsequently hired full-time. I am now working on adventitious agent safety and emerging technologies, all the while taking the technical, mentoring and intellectual skills from graduate school with me into this new role.

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

Apart from being a scientist I have a deep love and appreciation for the humanities – music and dance in particular. I marched in a competitive drum and bugle corps, and loved the life-long lessons and friends I made during that time. Some of these friends got together and we started a non-profit to promote diversity in the marching arts and provide scholarships. Recently, we even funded a theatre production and have expanded to hosting dance workshops.

Reference

Miller, J. C., Delzell, S. B., Concepción-Acevedo, J., Boucher, M. J. and Klingbeil, M. M. (2019). A DNA polymerization-independent role for mitochondrial DNA polymerase I-like protein C in African trypanosomes. *J. Cell Sci.* **133**, jcs233072. doi:10.1242/jcs.233072