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FIRST PERSON

First person – Laura Westrate

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. Laura Westrate is first author on 'Vesicular and uncoated Rab1-dependent cargo carriers facilitate ER to Golgi transport', published in JCS. Laura conducted the research described in this article while a post-doctoral fellow in Dr Gia Voeltz's lab at University of Colorado Boulder, CO, USA. She is now an Assistant Professor at Calvin University, Grand Rapids, MI, USA, investigating the mechanisms behind protein transport and sorting in the endoplasmic reticulum.

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

Mammalian cells contain different parts called organelles that have specific jobs. The endoplasmic reticulum (ER) is the largest cell organelle and the place where proteins are synthesized. It is estimated that about one third of all proteins made in mammalian cells are created and then exported from the ER. This transport is a multistep process that initiates at specialized sites on the ER called 'exit sites'. At these sites, the ER membrane is coated by specialized proteins, which help form a bud where cargo proteins are concentrated and packaged for export. These buds eventually excise as vesicles from the ER and travel through the cell to the next stop in the secretory pathway. Utilizing high-frame-rate live-cell fluorescence microscopy, we visualized cargo release events from exit sites in real time. We found that proteins known to coat and participate in the formation/maturation of the budding domain on the ER did not traffic away with the cargo as it leaves the ER. Instead, those proteins remained stably associated with the ER even after cargo had left, suggesting that, in animal cells, these proteins facilitate the formation of long-lasting hubs for cargo accumulation and export. Importantly, we provided a visual framework to further probe how these trafficking components regulate the stepwise handoff required for protein secretion. This is a pivotal step in overall cellular homeostasis.

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

One of the challenges associated with this project was the need to track secretory cargo in real time. We needed high temporal resolution in the acquisition of microscope images to ensure we could capture the dynamic export of cargo from the ER. To overcome this challenge, we focused on mammalian cells that were relatively flat to minimize the need for multiple *z*-steps in the acquisition process. We also chose to primarily use a spinning-disc confocal system to acquire thin optical sections at a much faster acquisition speed compared to a laser-scanning system. This allowed us to acquire triple-labeled fluorescent samples at the time scale needed to track cargo dynamics with confidence. Optimizing the triple fluorescence protein transfection was also challenging, as we needed to avoid cellular stress caused by the overexpression of exogenous proteins. We carefully chose the right transfection concentrations and tried several cargo monitoring systems to ensure that the behavior of cargo export we were witnessing was robust.

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Laura Westrate

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

One of the real 'eureka' moments was the first time I visualized cargo leaving a COPII marked site in real time under the microscope. The event wasn't obvious to me during the acquisition itself, but it jumped out right away when I started replaying the movie. We had been running with the working hypothesis that COPII components were stably associated with the ER but up until that point, we were still unsure of what that meant regarding the way that cargo was exported. It was exciting to see the cargo trafficking dynamics in real time, and it set the direction of our next experiments. We not only repeated and verified the event, but also determined what components were actually on the membrane cargo vesicle in lieu of COPII components.

> "It was exciting to see the cargo trafficking dynamics in real time, and it set the direction of our next experiments."

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

The Journal of Cell Science has built a strong reputation over the years of publishing high-quality articles encompassing a wide range of topics related to cell biology. Its wide audience base and its focus on significant topics in cell biology made it a perfect fit for our manuscript.

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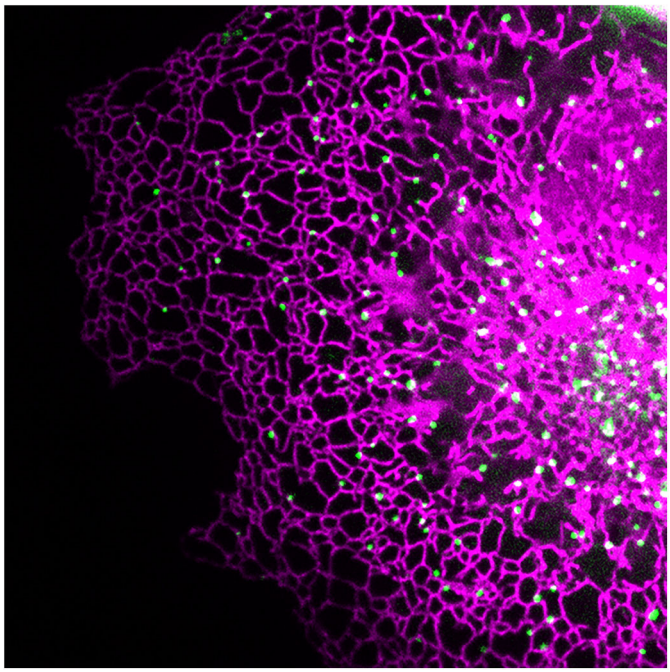

COPII proteins (green) mark exit sites distributed throughout the reticulated network of endoplasmic reticulum (magenta).

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

I've been lucky to have significant mentors at all three stages of my scientific training. Dr Moses Lee first introduced me to the possibilities of a career in research when I worked as an undergraduate in his lab. I was the first in my immediate family to go to college, and he provided the guidance and support I needed to take the necessary next steps in applying to graduate school. In graduate school, I found myself in an entirely new environment and my mentor, Dr Jeffrey MacKeigan, taught me how to take my general curiosity and refine it into a testable hypothesis that could advance our scientific understanding. He also gave me the freedom to pursue my own research interests, encouraging me to take risks and 'follow the science' even when it meant moving in a direction outside of the lab's expertise. As a postdoc, I needed someone who would advocate for me while also helping me develop the skills necessary to be successful in my own lab. My postdoc mentor, Dr Gia Voeltz provided that, while also helping me learn how to make the most of every opportunity that came my way. All of these lessons where important in my development into an independent scientist.

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 with the intricacies of the cell but it wasn't until graduate school when I first witnessed the dynamics of various cellular organelles under the microscope that I really narrowed down on the type of scientific research I wanted to do. I can remember being completely stunned that our textbook models for mitochondria or the endoplasmic reticulum looked nothing like what I was seeing under the microscope and I was immediately curious to learn more about how organelle morphologies were maintained and what function they played in maintaining organelle and cellular homeostasis.

"I can remember being completely stunned that our textbook models for mitochondria or the endoplasmic reticulum looked nothing like what I was seeing under the microscope…"

Who are your role models in science? Why?

I have a lot of role models in science, but one in particular that played an important role in developing my interest in science as a child was Jane Goodall. Not only did she share important lessons about conservation, but she also taught me how to be observant of my environment, using those observations to develop key questions about the world around me. As a woman, she was an important role model who demonstrated what it meant to follow your dreams even in uncharted territory. I grew up thinking I was going to be an explorer just like her and, while I may not be studying chimpanzees, I have tried to apply that explorer mentality in the lab as I seek to understand the intricacies of cell biology. One of my favorite quotes from her comes from her mother who had the following to say when she was encouraging Jane Goodall to pursue her dreams: "you'll have to work hard, take advantage of opportunities and never give up." It was an inspiration to me back when I was a little girl and it remains just as inspirational today.

What's next for you?

I just started as an Assistant Professor and have been enjoying the new challenges that come with managing teaching and starting up a research lab at a primary undergraduate institution. My short-term goals are focused on hitting milestones required for tenure while still playing an impactful role in the development of the next generation of scientists. I am excited to mentor students in the lab and help drive their curiosities in science as my previous mentors have done for me.

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

When I am not in the lab, I enjoy spending time outdoors hiking and taking photos of wildlife or various natural landscapes.

Reference

Westrate, L. M., Hoyer, M. J., Nash, M. J. and Voeltz, G. K. (2020). Vesicular and uncoated Rab1-dependent cargo carriers facilitate ER to Golgi transport. *J. Cell Sci.* **133**, jcs239814. doi:10.1242/jcs.239814