

FIRST PERSON

First person – Nicole Diggins

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. Nicole Diggins is the first author on ' $\alpha 5\beta 1$ integrin trafficking and Rac activation are regulated by APPL1 in a Rab5-dependent manner to inhibit cell migration', published in Journal of Cell Science. Nicole is a PhD student in the lab of Donna Webb at Vanderbilt University, Nashville, USA, investigating how the complex workings of the cell are disrupted by diseases such as viral infection or cancer.

How would you explain the main findings of your paper to non-scientific family and friends?

My lab studies the process of cell migration, which is how cells move. Cancer cells that migrate faster are associated with metastasis, which leads to poor prognosis in the patient. My main PhD project has focused on the role of a protein called APPL1 in cell migration. APPL1 has many functions in the cell, including regulation of cell migration, but we don't entirely understand how APPL1 does this. An interesting aspect of APPL1 is that the protein interacts with a lot of other proteins, and can be important for both how proteins move within the cell and how proteins send signals that make the cell move. This paper shows that APPL1 inhibits cell migration by changing two processes important to cell migration: integrin trafficking and Rac signalling. Integrins are proteins on the outside of the cell that help act as the 'feet' for cellular movement, and APPL1 changes how these proteins are moved within the cell. Rac is a protein that helps send signals within the cell to make it migrate faster, and APPL1 stops Rac from doing this.

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

While I was in the process of writing this paper for publication, my thesis advisor, Dr Donna Webb, passed away. Dr Webb had been sick for some time, and so I had been mostly writing the manuscript on my own. Unfortunately, she wasn't able to read the entire paper, and so I never received her feedback to help with its publication. When I received the reviews on the paper, I spent several months performing experiments to address the reviewers' concerns in a lab that was in the process of shutting down. Many of my lab mates had already moved on to other labs, and so I was lacking a lot of the support I would normally have, had my advisor still been here.

"I would urge students early in their training to identify what kind of mentor will be the most beneficial to them and what scientific questions interest them the most."

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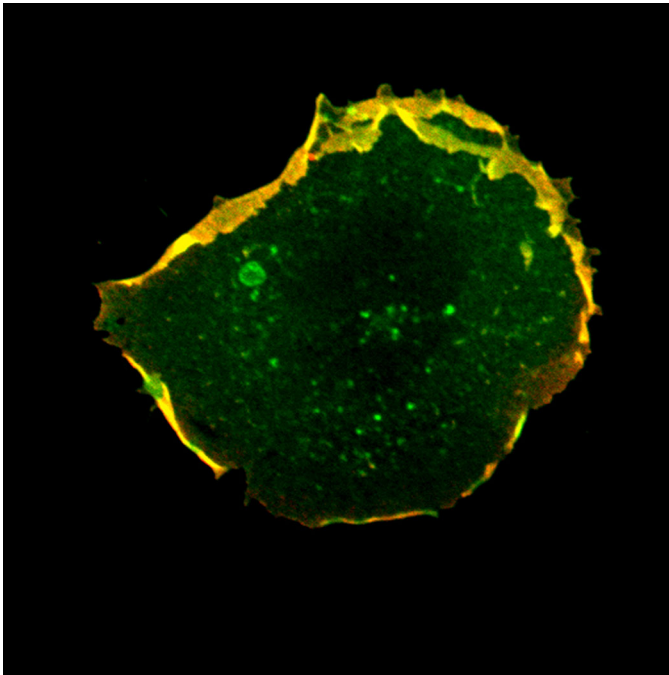
Nicole Diggins

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

I had a hypothesis that APPL1 regulated integrin trafficking, but my lab had never studied this process. I had done a lot of literature searches and read a great deal about this field of research, but when I started optimising integrin internalisation assays, I really had no idea if it would work. And I wasn't sure, if the experiment did work, whether there would be any differences in integrin trafficking when I changed APPL1 expression levels. When I first observed that APPL1 overexpression decreased integrin internalization, that was my 'eureka' moment, when I knew that this project would take off and tell an important story.

Have you had any significant mentors, and how have they helped you?

I have had a few mentors that have been key in publishing this paper, as well as in my training as a graduate student. Dr Donna Webb, my thesis advisor, was important in setting up this project and my early development as a graduate student. Sadly, she passed away before seeing this project come to completion. I am also eternally thankful to Dr Kathy Friedman from the Department of Biological Sciences at Vanderbilt, for stepping in as my advisor for the completion of my graduate studies, and for helping with the submission of this paper. I am also grateful to Dr Alissa Weaver from the Department of Cell and Developmental Biology in the Vanderbilt School of Medicine, who helped guide me through experiments needed for the revisions



HT1080 cell stained for β 1 integrin expression as part of investigations into the effect of APPL1 on integrin trafficking. Total integrin is shown in red (non-permeabilised) and internalised integrin is green (permeabilised). Yellow (overlay) shows integrin on the cell surface.

to the paper, and supported my science as the Webb lab was in the process of closing.

What's the most important piece of advice you would give first-year PhD students?

The most important decision a first-year PhD student can make is what lab to join. I would urge students early in their training to identify what kind of mentor will be the most beneficial to them and what scientific questions interest them the most. Additionally, I

would encourage first-year PhD students to find resources outside of the lab that will help them with their training, including additional mentors, people with expertise in their field or methods they will need in their project, and the emotional support to get them through years of graduate school.

What changes do you think could improve the professional lives of early-career scientists?

I think that graduate students have a lot of support early in their training, but more efforts could be made to help students in completing their PhD and transitioning to their next career step, whether or not they continue in academia.

What's next for you?

After I complete my PhD, I will be moving on to a postdoctoral position at Oregon Health and Science University, where my project will focus on the regulation of the Rho pathway by human cytomegalovirus miRNAs in viral latency and haematopoiesis.

“I believe that balancing your professional and personal lives is crucial to maintaining a healthy lifestyle.”

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

I am an advocate for a healthy work/life balance. I believe in working hard in the lab to answer scientific questions and foster learning and discovery. When I am not in the lab, I have many hobbies, including hiking, running, crocheting, seeing movies and playing with my cats. I believe that balancing your professional and personal lives is crucial to maintaining a healthy lifestyle.

Reference

Diggins, N. L., Kang, H., Weaver, A. and Webb, D. J. (2018). α 5 β 1 integrin trafficking and Rac activation are regulated by APPL1 in a Rab5-dependent manner to inhibit cell migration. *J. Cell Sci.* **131**, jcs207019.