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FIRST PERSON

First person – Seth Zimmerman

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. Seth Zimmerman is the first author on 'Cells lay their own tracks – optogenetic Cdc42 activation stimulates fibronectin deposition supporting directed migration', published in Journal of Cell Science. Seth completed the work in this article as a PhD student under the supervision of Jim Bear and Brian Kuhlman at University of North Carolina at Chapel Hill, USA. He is currently a postdoc in Chris Counter's laboratory at Duke University in Durham, North Carolina, USA, investigating the basic cell biology of cancer and metastasis, and designing new approaches to study it.

Seth Zimmerman

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

When friends and family ask what I work on I usually tell them that I'm engineering laser-guided remote control cells. That at least sparks their interest, but they often ask what the purpose is. I then follow up by telling them that cell migration is essential for many aspects of life, yet we still don't fully understand how and why cells move from one place to another. For instance, we know that in part, cells move by extending protrusions and pulling themselves along. However, we don't know the details of how the cell coordinates the protrusion and what molecular components contribute to the process. With our engineered tools, we can shine a laser on a part of a cell and initiate a cell protrusion by a specific molecular means. Since we know the molecule through which we induced the protrusion, we can relate the cell's molecular and physiological response directly to the activity of the initiating molecule. In our paper, we used this logic to dissect the contributions of two similar molecules to protrusion and directional migration.

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

This project presented many challenges. The largest challenge, though, was to find an interesting question to ask. The project started out as a proof of concept for our light-inducible dimer. The purpose of the dimer was to be a tool used to answer interesting questions, but we did not have a specific question in mind when designing it. It was like designing a hammer to drive a nail without knowing what we were going to build. To find an interesting question, I started using the GEF-fused dimers in many different assays, trying to find interesting differences in how the switches behaved. Eventually, I came across the difference in response to ECM concentrations.

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

The largest surprise from this research was twofold. First, I did not expect such a binary response to different fibronectin concentrations when inducing a protrusion by stimulating Rac activity. I expected a graded response (i.e. as the concentration of fibronectin gradually lessened so would the protrusion size). Instead, we found that depending on the concentration of fibronectin, either the cell fully protruded or failed to protrude, but nothing in between. I had never seen such a black-and-white response in biology, where things are usually grey. Second, and possibly more surprising, was when I realized that Cdc42-induced protrusions did not behave in the same way. They protruded independently of the fibronectin concentration. This is when things really got interesting.

> **"I had never seen such a black-and-white response in biology, where things are usually grey."**

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

I've been lucky enough to have nothing but significant mentors. For this work, though, I was co-mentored, and Jim Bear and Brian Kuhlman have both been great. I can imagine that it is difficult to have a student that is being pulled in other directions by another mentor. However, Jim and Brian trusted me enough to

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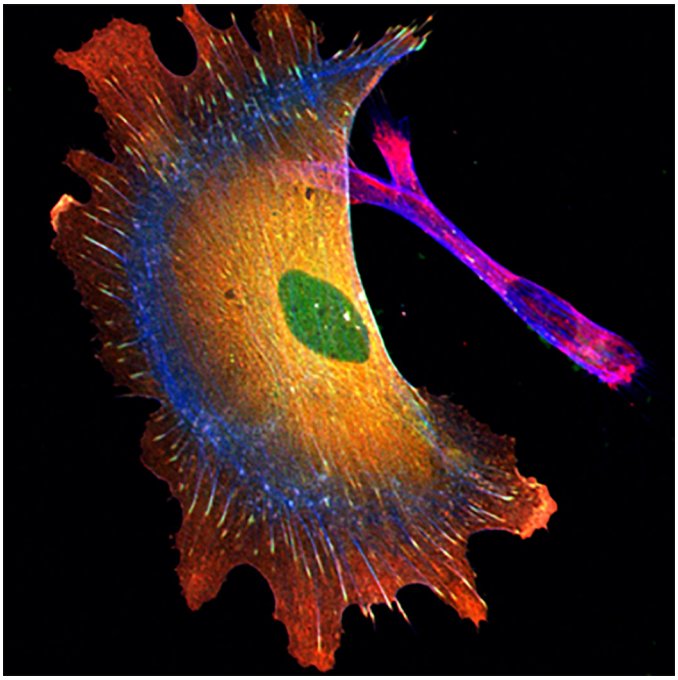

A fibroblast stained for paxillin (green), actin (blue) and Venus-iLID-CAAX protein (red).

give me lots of room to explore yet knew the right times to give advice.

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

Have fun. Grad school can be stressful at times and you certainly aren't compensated for it. Therefore, you need to really like what you are doing, otherwise the next 4–7 years will be miserable. The lab is usually a fun place to be, but if you find yourself in a funk and don't like being there, take a time-out and get out of the lab. Also, break up some of the monotony with fun new experiments or ideas.

"The lab is usually a fun place to be, but if you find yourself in a funk and don't like being there, take a time-out and get out of the lab."

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

Management training. I think it is the goal of many early-career scientists to one day run their own academic lab or be a project manager for a company. I think that scientific training teaches none of the management skills necessary to do these jobs. It seems like there is a huge burden on new PIs when they are thrown into that position and don't know how to manage and interact with people but are expected to learn on the job. Sometimes they never learn these skills, which can significantly impact the research in their lab.

What's next for you?

I have recently started a postdoc position at Duke University.

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

Science was my least favourite subject in grade school. I think it was because science was taught as a series of facts and you didn't really learn much about the process of science.

Reference

Zimmerman, S. P., Asokan, S. B., Kuhlman, B. and Bear, J. E. (2017). Cells lay their own tracks – optogenetic Cdc42 activation stimulates fibronectin deposition supporting directed migration. *J. Cell Sci.* **130**, 2971-2983.