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First person – Michael Shannon

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. Michael Shannon is first author on 'Differential nanoscale organisation of LFA-1 modulates T-cell migration', published in JCS. Michael conducted the research described in this article while a PhD student in Dr Dylan Owen's lab at the Randall Biophysics Dept, King's College London, UK. He is now a postdoc in the lab of Dr Emily Mace at the Department of Pediatrics Infectious Diseases, Columbia University Irving Medical Center working on natural killer cell development.

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

T-cells are great at multiple forms of migration, but the mechanics of this are not fully known. Some forms of T-cell migration involve a well-characterized flow of the actin cytoskeleton, like the engine in a car, to the outside environment via integrins. These integrins are like hooks, which translate the force of the flowing actin into forward movement, by attaching to other proteins outside the cell. We know that the spatial organization of integrins is really important, and that they form clusters, little signalling islands that modulate the strength of the attachment. Regular imaging techniques have only allowed a surface investigation of these clusters. With new super-resolution microscopy techniques, coupled to cluster analysis techniques that rely on less human decision making, we were able to characterize the organization of these proteins into nanoclusters. Interestingly, we found that the nanoclusters arranged into different sizes and densities depending on their location in the cell membrane. We also found that the clusters changed size and density depending on the speed of the cell. Using semi-correlative live cell-to-fixed cell experiments, we were able to show that cell speed, the attachment of actin, and the size of clusters are all linked. I'm sure that in the future, manipulating some of these aspects will allow us to answer questions about how our immune system works as a whole, and how nanoscale events can influence macroscale changes to the system.

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

The project required a lot of manual imaging to get the sample size required for us to be sure that the changes we were seeing were consistent. We deliberately chose a heterogeneous source of T-cells (from mice, with a quite general stimulatory or proliferatory signal) in order to discover generalizable phenomena across T cells. This meant that to be sure of the changes, we had to image many cells. New high-throughput techniques are being introduced all the time, including techniques to recognize cells and image them automatically – I think this side of things is the future of this kind of quantitative microscopy.

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Michael Shannon

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

When we saw conserved, very clear changes in cluster patterns in separate parts of the cell! Also when we saw that the size and density versus speed changes are conserved too, and that known active adhesion markers were spatially more present on the nanoscale in the faster cells. It was amazing to see evidence that nanoscale events could change whole-cell behaviors.

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

Our research fits really well into a theme associated with super-resolution microscopy and its applications to biological problems. Also, we knew that JCS has a wide readership – in general this kind of work is becoming more multi-disciplinary, so wide access was important for us.

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

Dylan and Georgina, as well as all of the members of the Randall department at King's College London, are excellent friends as well as colleagues. Many, many visits to the pubs of London Bridge with them made it a really special time.

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?

It was a winding road. I started off with philosophy and French, before switching and doing biochemistry, followed by biophysics in

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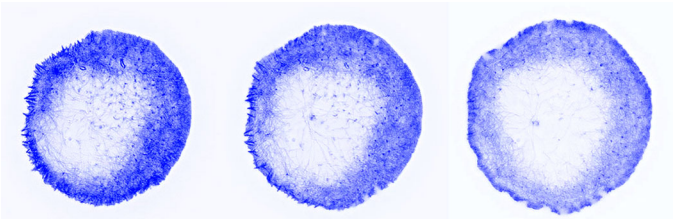

NK cell spreading out as it forms a synapse. An image related to my current research. This is a human NK cell expressing LifeAct mScarlet undergoing dynamic actin rearrangement as it undergoes spreading on a functionalized surface imaged via SIM-TIRF microscopy. Image acquired in the laboratory of Emily Mace at the Columbia University Irving Medical Center.

a cryo EM lab. Then, I moved to super-resolution microscopy, via molecular biology (protein engineering) in Japan. Now I'm doing a mix of the latter two, to investigate NK cell development. Shout out to the whole Mace lab at Columbia! Peter Rosenthal (then at the NIMR, now at the Crick) was an excellent tutor at an early stage. He listened to me and made me feel like a career in research might be up my alley. I loved the machines I was allowed to work with (vitrobots, polara electron microscopes), and grew in confidence. Doing rotation projects with Anne Ridley, Maddy Parsons and a PhD with Dylan were all really amazing. Alongside using my opportunities fearlessly, I'm interested in deconstructing how I was able to get those opportunities, whereas others were not.

Who are your role models in science? Why?

Octavia Butler, for her writings of alien species with different societies to ours (I hope sci-fi counts!).

What's next for you?

Right now, I'm working as a postdoc in Emily Mace's lab at Columbia in New York. Scientifically, we look at natural killer cell development, and how that influences their killing of cancerous or virally infected cells. We are going to be using living tissues and organoids as environments and development platforms to identify *in vivo* relevant behaviors by high- or super-resolution microscopy. There are lots and lots of samples from patients and a multi-disciplinary team who are all pretty excited about the future of the field.

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

I'm currently learning about ways in which I can use the enormous privilege of being scientifically literate to subvert an overwhelmingly discriminatory wider system. Doing science is context specific, and is part of yet another system that needs to be decolonized.

Reference

Shannon, M. J., Pineau, J., Griffié, J., Aaron, J., Peel, T., Williamson, D. J., Zamoyska, R., Cope, A. P., Cornish, G. H. and Owen, D. M. (2020). Differential nanoscale organisation of LFA-1 modulates T-cell migration. *J. Cell Sci.* **133**, jcs232991. doi:10.1242/jcs.232991