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FIRST PERSON

First person – Clara Mutschler

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Clara Mutschler is first author on 'Schwann cells are axo-protective after injury irrespective of myelination status in mouse Schwann cell–neuron cocultures', published in JCS. Clara is a PhD student in the lab of Peter Arthur-Farraj at the John Van Geest Centre for Brain Repair, University of Cambridge, UK, investigating axon–Schwann cell interactions after peripheral nervous system injury.

Clara Mutschler

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

Signals in the nerves throughout our body need to be sent around quickly, so we can respond to everything going on around us. To allow this quick signal transmission, our nerves are insulated – or myelinated. We developed a system where we can culture nerve cells with the type of cells that provide this insulation, Schwann cells. These Schwann cells can then myelinate the nerve fibres, and we can investigate how they do this, or what happens after injury in this model.

We show that our cocultures behave like the cells in our body do after injury in a few ways, and interestingly the Schwann cells slow down degeneration of nerve fibres. They have this protective effect not only when they are myelinating, but also when they are not myelinating and are just aligned to the nerve fibres. Importantly, in our cultures, we only use mouse cells (as mice are a common animal model used in this field), and we can now use cells from different mouse models and separately manipulate neurons and Schwann cells. Hopefully this will, in the long term, allow us to better understand what happens in our nerves after injury and how different cells interact with each other in this context.

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

This is one of those projects that got just a tiny bit delayed by the pandemic. We had a beautiful set of 40 cultures going, and then the first lockdown happened, resulting in the lab being closed for several months! I was unable to set up any cocultures for over a year as the work was not compatible with the reduced working hours and the shift system we were using. During that time, I was also not able to work across different university departments, and I normally set up the cocultures in a different building to the one I had access to at the time. So, I am super happy to now finally see the work published!

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

The most exciting moment on this project was probably being able to watch Schwann cells ingest and digest axons. I wanted to see if I could live image our Schwann cell–dorsal root ganglion neuron cocultures, and monitor the interaction of Schwann cells and axons to see whether there were any interesting morphological changes. Setting up long-term live imaging is always challenging, as you need to make sure the sample doesn't drift out of focus and that the conditions are just right so the cells stay happy and healthy. I had imaged a few cocultures for up to 12 h but wanted to try to keep them going for a bit longer and image for a whole 48 h. When I went back in to check on the cultures, I was super excited to see they were doing well, were still in focus, and I had some really cool movies of Schwann cells fragmenting, ingesting and digesting axons!

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

We wanted to try submitting to Review Commons, as we usually preprint our work and like the idea of journal-independent peer review to potentially save a paper from being reviewed more than once at different journals. The Company of Biologists' journals allow transfers from Review Commons, and we thought Journal of Cell Science would be an excellent home for our paper, especially as they have published many incredibly interesting tools and techniques in the past.

What's next for you?

I am wrapping up my PhD and have just submitted my thesis! Now I've got lots of exciting work to look forward to as a postdoc here in Cambridge. I'm excited to continue learning about all the different ways in which neurons and glial cells interact, and I can't wait to see where this work will take me.

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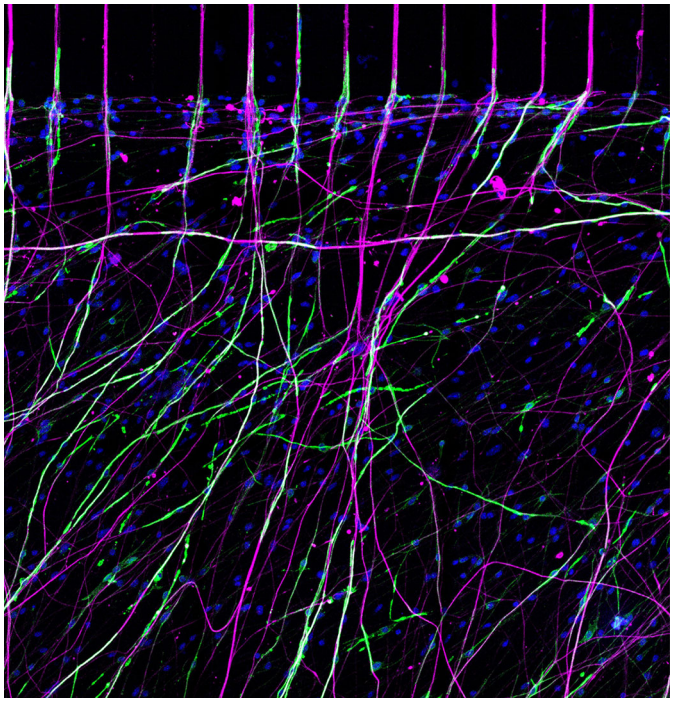

Myelination in a compartmentalised murine Schwann cell–dorsal root ganglion neuron coculture in microfluidic chambers. Myelin-associated protein periaxin-labelled myelin segments (green) cover neurofilament light chain-labelled axons (magenta). Nuclei are labelled in blue using DAPI. These cocultures allow separate genetic manipulation of mouse Schwann cells or neurons, use of cells from different transgenic animals, axotomies to study injury, and drug treatments in a purely murine culture with robust myelination. Schwann cells protect axons after injury in these cocultures and delay axon degeneration, irrespective of whether they are myelinating or not.

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

I love baking – and every supervisor I've had has asked why I am doing science and not opening a bakery instead! I've made wedding cakes for my siblings, I've baked a brain cake (it looked disgustingly realistic) and a cell cake, and I've even made a croquembouche for one of my co-authors on this paper (and transported it across London on the Tube). I'm currently planning a nerve cross-section cake, where I want to draw all the myelinated axons of a nerve cross-section on a cake and then mirror glaze it, so it looks a bit like a nerve sample.

What is your scientific background and the general focus of your research?

I studied neuroscience as an undergraduate student and was fascinated by how cells interact with each other, and especially how neurons interact with glia and how this regulates the function of both neurons and glia. I then started my PhD at the University of Cambridge investigating axon–Schwann cell interactions, specifically after peripheral nervous system injury. After injury, axons degenerate and Schwann cells transform into repair Schwann cells, which digest myelin, attract macrophages, and support neuronal survival and axon regeneration. Both axon degeneration and this repair process are regulated by cell-intrinsic molecular pathways, but their interaction and the Schwann cell injury response are incompletely understood. I am working on further characterising this injury response and on understanding the transcriptional changes in Schwann cells after nerve injury. As a part of this work, I have used a range of different model systems, including the cocultures described in our paper, but also mice and zebrafish.

Reference

Mutschler, C., Fazal, S. V., Schumacher, N., Loreto, A., Coleman, M. P. and Arthur-Farraj, P. (2023). Schwann cells are axo-protective after injury irrespective of myelination status in mouse Schwann cell–neuron cocultures. *J. Cell Sci.* **136**, jcs261557. doi:10.1242/jcs.261557