

FIRST PERSON

First person – Richard Eva

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. Richard Eva is the first author on 'EFA6 regulates selective polarised transport and axon regeneration from the axon initial segment', published in Journal of Cell Science. Richard is a research associate in the laboratory of Prof. James Fawcett, investigating the intrinsic mechanisms preventing brain and spinal cord axons from regenerating after injury in order to identify novel strategies for enhancing repair.

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

Injuries to the brain or spinal cord cause damage to the nerve fibres (axons) that connect the brain with the body. This causes paralysis because these axons do not regrow after injury. We wanted to find out why the axons do not regrow in order to find new treatments to reconnect injured fibres and restore function. Our research shows that the reason axons don't regenerate is that the machinery needed for growth is restricted to a part of nerve cells that is far away from the axons. Growth machinery is kept in cell bodies and not transported into axons. We found a protein, EFA6, which acts as a gatekeeper, sending growth machinery away from axons by switching on another protein, ARF6. We further discovered that removing EFA6 allowed growth machinery into axons. These results show that EFA6 and ARF6 control regeneration, suggesting that they could be targets for treating brain or spinal cord injury. There is a lot to do before this can lead to treatments, but it is an exciting step forwards.

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

The 'eureka' moment was finding the ARF6 activator EFA6 in the axon initial segment (AIS). A goal of my research has been to find ways of allowing integrins to be transported into central nervous system axons. At the time, I was doing experiments to establish that axonal integrin transport was regulated by ARF6, while the lab was interested in the idea that the AIS might also control axonal integrin transport, functioning (through an unknown mechanism) as a barrier to the axon. I read a paper which demonstrated that ARF6 can control the direction of transport along microtubules depending on its activation state. I was excited by the idea that there might be an ARF6 activator in the AIS that would cause integrins to be retrogradely transported away from axons. It would also explain how signalling could regulate transport from the start of the axon. I was initially disappointed when the first molecule we looked at was expressed throughout the axon, but relieved when I first examined the immunofluorescence staining for EFA6, to find it was strongly enriched in the AIS.

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Richard Eva

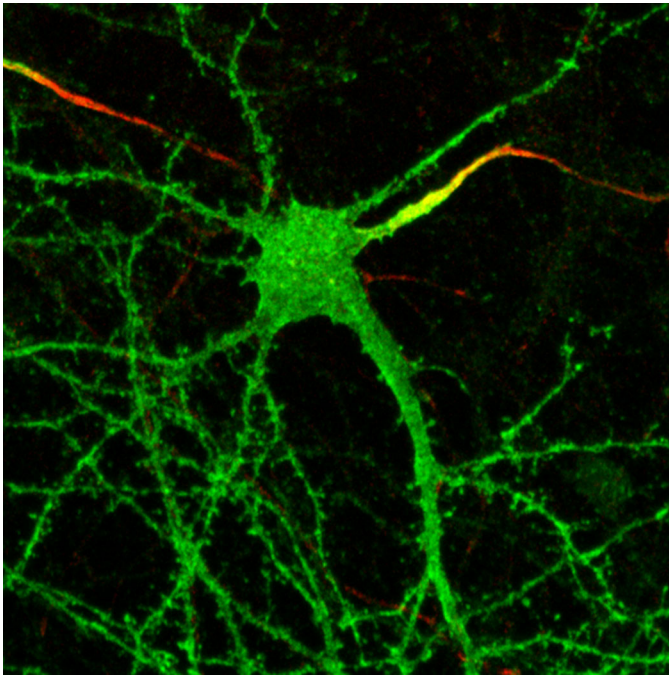
“Focus on the experiments you're doing and the targets you have – there are lots of ways to be distracted by 'look see' experiments.”

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

Be organised and focused, and accept that you are on a learning curve to avoid being disappointed when techniques don't work out. Don't expect to be an expert overnight, it may take you a few goes before you get good at a particular technique. Organisation and planning are really important to keep things moving forward. Focus on the experiments you're doing and the targets you have – there are lots of ways to be distracted by 'look see' experiments, which can be exciting but are also high risk. Three years goes quickly, and you don't want to waste time. Repeating experiments carefully may seem boring but will get you solid data.

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

A defined career path and more funding aimed at the post doc and early-career level. It seems there is funding available for early-career researchers who already have their foot on the ladder, but it is very difficult to get on the ladder with few tenure-track fellowships available. Moving beyond post docs towards an independent position is extremely challenging.



EFA6 (green) in cortical neurons in culture.

What's next for you?

Moving towards an independent career. I am continuing to investigate axon transport as a target for boosting axon regeneration in the injured nervous system, and will be testing the approaches described in our paper in relevant models of injury. In addition to this, I'm investigating the upstream signalling pathways that control transport and regeneration using the techniques in the paper as well as relevant models. Beyond that, there are a host of trafficking and transport investigations I'd like to do in both the regeneration and degenerations fields, but they will remain top secret for now.

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

I have a classic 1980s Pearl BLX drum kit which is perfect for playing 'In the air tonight' by Phil Collins (it's not bad for music from this century too!).

Reference

Eva, R., Koseki, H., Kanamarlapudi, V. and Fawcett, J. W. (2017). EFA6 regulates selective polarised transport and axon regeneration from the axon initial segment. *J. Cell Sci.* **130**, 3663-3675.