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FIRST PERSON

First person – Natalie Farrawell

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. Natalie Farrawell is the first author on 'SOD1^{A4V} aggregation alters ubiquitin homeostasis in a cell model of ALS', published in Journal of Cell Science. Natalie is a Senior Research Assistant in the lab of Justin Yerbury at the Illawarra Health and Medical Research Institute, University of Wollongong, Australia, investigating the molecular processes underpinning amyotrophic lateral sclerosis (ALS), with a particular emphasis on protein misfolding, protein aggregation and inclusion formation.

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

Inside each of the cells within our body are millions of protein molecules bustling about and working hard. Proteins have many functions; for example, they can be used as building blocks or transporters. Various molecular systems within cells recognise whether or not proteins are functioning normally. When proteins are damaged and cannot function normally, an important cellular garbage disposal system is called upon.

Ubiquitin is the molecule responsible for targeting damaged proteins to the cells' garbage disposal machinery. In amyotrophic lateral sclerosis (ALS, also known as motor neurone disease or Lou Gehrig's disease), damaged proteins accumulate and form toxic deposits called inclusions that can't be disposed of by the cell very quickly. In our study, we found that these inclusions contain large amounts of ubiquitin, which means that the levels of free ubiquitin within the cell are compromised and the cellular garbage disposal system is perturbed, eventually leading to cell death.

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

Working in science is a constant challenge; there are lots of obstacles that you have to overcome. In this project, I used a technique called FRAP (fluorescence recovery after photobleaching) to watch where the free ubiquitin was moving in the cell. First, we performed FRAP on cells expressing mRFP-tagged ubiquitin, but mRFP is very susceptible to photobleaching so we had trouble measuring its recovery. We had a lot more success once we replaced mRFP with the more photostable mCherry tag. Also, cells liked to dance around when I needed them to sit still under the microscope. This makes imaging them very difficult, but even I find it hard to sit still when Ricky Martin songs are playing in the lab!

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

Getting the FRAP experiments to finally work for this paper was one of them, but I think the biggest 'eureka' moment was seeing all the data come together to support our hypothesis regarding ubiquitin-proteasome system dysfunction in ALS.

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Natalie Farrawell

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

If the shoe fits, wear it! Journal of Cell Science has a strong reputation in cell biology so we're hoping to share our research far and wide.

"…I think the biggest 'eureka' moment was seeing all the data come together to support our hypothesis regarding ubiquitin-proteasome system dysfunction in ALS."

Have you had any significant mentors who have helped you beyond supervision in the lab?

Absolutely. My research supervisors Prof. Justin Yerbury and Prof. Mark Wilson have always provided me with sound advice, both in life and science. Mark has a way of being brutally honest while Justin is a constant source of encouragement. I've worked with them for more than five years now and they've given me countless opportunities to grow and become a better scientist.

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?

I had an exceptional science teacher at school. She made science fun, so science was on my mind from an early age. My interest in neuroscience and neurological disease started when my

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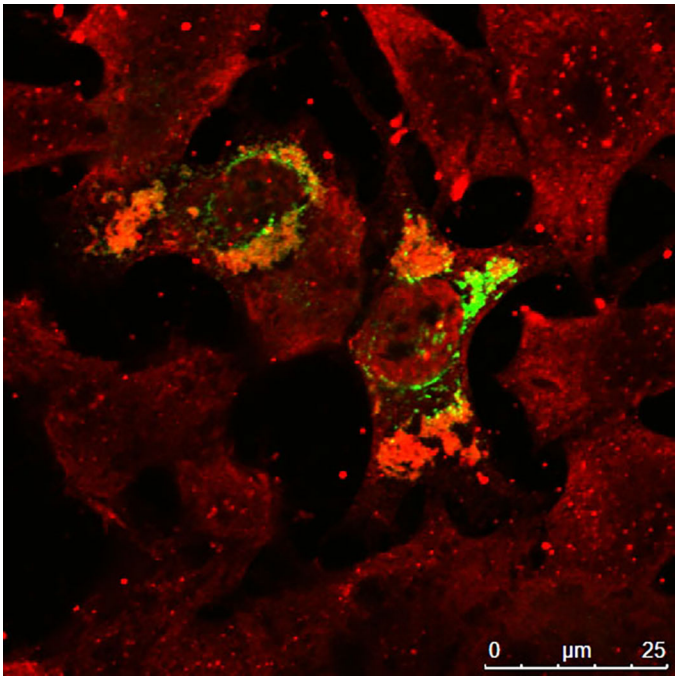

Neuronal (NSC-34) cells expressing ALS-associated mutant FUS (green) and stained for ubiquitin (red)

grandmother was diagnosed with Alzheimer's disease. There is nothing more motivating than watching someone you love suffer. If I can make even a small difference to help ease the suffering of others, and give people some hope, it will all be worthwhile.

"If I can make even a small difference to help ease the suffering of others, and give people some hope, it will all be worthwhile."

Who are your role models in science? Why?

Justin Yerbury. Not only is he a brilliant scientist, but he's an inspirational human being. Under circumstances that would deter most people, Justin has soldiered on to become a world leader in ALS research. His dedication and passion for research is something that I and many others admire.

What's next for you?

I'm going to Russia for a holiday soon, but when I get back I'm going to continue to try to find a cure for this insidious disease.

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

I'm learning to surf, but my favourite days are spent fishing with my dad and grandpa in Mystery Bay.

Reference

Farrawell, N. E., Lambert-Smith, I., Mitchell, K., McKenna, J., McAlary, L., Ciryam, P., Vine, K. L., Saunders, D. N. and Yerbury, J. J. (2018). SOD1^{A4V} aggregation alters ubiquitin homeostasis in a cell model of ALS. *J. Cell Sci.* **131**, jcs209122.