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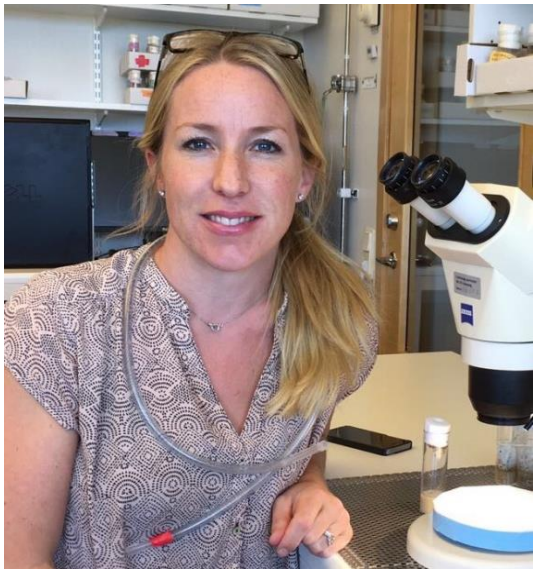
FIRST PERSON

First person – Josefin Fernius

First Person is a series of interviews with the first authors of a selection of papers published in Disease Models & Mechanisms, helping early-career researchers promote themselves alongside their papers. Josefin Fernius is first author on 'Bar-coding neurodegeneration: identifying subcellular effects of human neurodegenerative disease proteins using *Drosophila* leg neurons', published in DMM. Dr Fernius is a post-doc in the Department of Clinical and Experimental Medicine at Linköping University, Sweden, investigating the function of F-actin in the pathogenesis of neurodegenerative disease.



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

We wanted to create a system for easy analysis of a broad range of functions of nerve cells, and in particular the axons, which are the very long projections of nerve cells enabling communication between, for example, a muscle and the central nervous system. Using adult leg nerve cells of the fruit fly (*Drosophila*) as a model system, we labelled different structures within these cells with fluorescent molecules, then analyzed whether these structures changed when exposed to different human proteins that are linked to neurodegenerative diseases, like Alzheimer's or Huntington's disease. We observed a variety of interesting effects, including toxicity, mobility defects, premature death and also specific effects on certain cellular structures. Interestingly, most, but not all, human disease proteins we tested caused changes in F-actin filament structures. F-actin is part of the cells' cytoskeletal backbone, which plays several key roles in nerve cells, e.g. as a cellular scaffold important for cell shape, but also has other important roles in nerve cell signal transmission.

"We believe that *Drosophila* still holds enormous potential for [neurodegenerative disease research], as long as the right scientific questions are asked."

What are the potential implications of these results for your field of research?

We believe that we have developed a useful method where one can test a number of known or candidate disease proteins, and evaluate specific neuronal effects in a time- and cost-efficient manner. Although some of our results with already-published disease proteins were anticipated and with markers that have earlier been investigated in different settings, we also found novel effects on the F-actin cytoskeleton, which will be exciting to explore further. The role of F-actin in neurodegenerative disease is relatively understudied, and we believe our results are a promising ground for further study and potential therapies for neurodegenerative diseases.

What are the main advantages and drawbacks of the model system you have used as it relates to the disease you are investigating?

Historically, the fruit fly has been an invaluable tool for studying human neurodegenerative disease mechanisms due to its fast generation time, low-cost maintenance and extensive genetic tools, leading to major discoveries within the field. With the rapidly emerging technology of CRISPR etc., enabling relatively straightforward genomic editing even in mouse, the benefits of using *Drosophila* are under scrutiny. Importantly however, with an increase in the ageing population and expectations that this will become the greatest burden for public health, the need for rapid methods to study neuronal disease mechanisms and prevention, becomes even more urgent. We believe that *Drosophila* still holds enormous potential for this purpose, as long as the right scientific questions are asked.

What has surprised you the most while conducting your research?

We used a range of fluorescently tagged proteins and analysis of them gave rise to robust and interesting labelling of different structures, reporting on a variety of functions in fly leg neurons. Most of them gave anticipated labelling, yet gave interesting results upon exposure to neurodegenerative disease proteins. However, one of them, Lifeact-Ruby, which labels F-actin, revealed an unexpected labelling of the initial part of the axon, close to the sensory neuron cell body. Moreover, this F-actin structure was found to be severely affected in flies expressing some of the disease proteins. This

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interesting result paves the way for future analysis of the role of this structure in disease, and I look forward to investigating this further.

Describe what you think is the most significant challenge impacting your research at this time and how will this be addressed over the next 10 years?

Considering the social burden of neurodegenerative diseases and the present lack of effective therapies despite enormous research efforts, we are facing a huge challenge in this research community. Finding the true culprit in these diseases has been extremely difficult. For example, it is well-established that both amyloid beta and Tau are involved in Alzheimer's disease; however, the etiology of this disease is extremely complex and finding the early, triggering events has proven tricky. Animal models remain pivotal in the understanding of neurodegenerative disease, and for identification of new therapeutic strategies. I believe that it is also important to focus research efforts into understanding the normal, aging processes of neurons, before applying it to disease. Unfortunately, however, funding bodies are increasingly focusing their support on *in vitro* studies, rather than on high-resolution *in vivo* models, which I believe will be detrimental for the discovery process and indeed for the development of novel therapeutic strategies. We try to address this by using a simple *in vivo* neuronal model to study normal and aging processes of neurons. Yet, this system also allows controlled introduction of aggregating proteins to follow early and late events of such insults, and we hope this could reveal novel targets to interfere with disease.

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

I believe networking facilities at universities, similar to those for PhD students, would be beneficial for post-docs in their early career. Meetings would be useful for discussing career paths, grant writing and topics of general concerns for post-docs.

What's next for you?

My immediate scientific goals are to further develop this model to unravel the complex function of F-actin in the pathogenesis of neurodegenerative disease. Professionally, I am looking forward to taking the next step in my career, and helping the next generation of early career researchers to contribute to research on neurodegenerative disease.

Reference

Fernius, J., Starkenberg, A. and Thor, S. (2017). Bar-coding neurodegeneration: identifying subcellular effects of human neurodegenerative disease proteins using *Drosophila* leg neurons. *Dis. Model. Mech.* **10**, doi: 10.1242/dmm.029637.