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FIRST PERSON

First person – Luke Thompson

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. Luke Thompson is the first author on 'Neurochondrin interacts with the SMN protein suggesting a novel mechanism for spinal muscular atrophy pathology', published in Journal of Cell Science. Luke conducted the research in this article while a PhD student in the lab of Dr Judith Sleeman at the University of St Andrews, UK. He will be joining Prof. Elliot Androphy's lab group at Indiana University, USA, as a postdoctoral fellow, investigating the role of the coatomer proteins and associated factors in neuronal function.

Luke Thompson

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

Although the cause of spinal muscular atrophy (SMA), a reduction in the amount of functional survival of motor neurone protein (SMN), has been known since the 1990s, it is still far from clear exactly why this disease predominantly affects motor neurons, as SMN is an essential protein involved in 'housekeeping' – looking after the maintenance and survival of the cell. One potential theory is that SMN has a specific additional role in neurons: helping to transport RNA to the ends of neurons, in a similar way to a delivery van transporting a product from a distribution centre to its final destination. Previous lab research has indicated that this transport occurs in vesicles (lipid-rich structures) alongside SNRPB, another protein involved in the essential housekeeping role of SMN. In our paper, we have built on this, identifying that a protein related to SNRPB, called SNRPN, may also be involved. Additionally, we identified another protein that interacts with SMN, neurochondrin (NCDN). NCDN expression may influence where SMN is localised within cells, and vice versa, so this interaction could be an important new target for drugs to help treat SMA in the future.

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

We used mainly SH-SY5Y cells, a neuroblastoma cell line, for much of this project. Although they express NCDN, it was not usually at a high level, making immunodetection of endogenous NCDN occasionally difficult. Additionally, the lipid structures identified in this project were disrupted by the permeabilisation used in immunocytochemistry, making imaging and determining colocalisation difficult. To get around these problems, we produced cell lines that constitutively expressed low amounts of GFP- or mCherry-tagged proteins to allow better detection and better observation of colocalisation in the lipid-rich structures where required.

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

The eureka moment came after producing the NCDN–GFP plasmid, when the tagged protein co-immunoprecipitated SNRPB, as well as colocalising with SNRPB and SNRPN in the neurites of cells. As well as this, the co-immunoprecipitation and colocalisation with SMN confirmed that this was an interesting newly discovered interaction.

Have you had any significant mentors, and how have they helped you?

My PhD supervisor, Dr Judith Sleeman, has been very supportive throughout my PhD. She helped me to become better at many lab techniques and provided advice on where to go with the project, but also allowed me to shape the project in my own way.

> **"[…] you will learn and hone lots of skills that will be useful for the rest of your life, both inside and outside the lab"**

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

Be prepared to learn a lot, particularly in your first few months! Throughout your PhD, you will learn and hone lots of skills that will be useful for the rest of your life, both inside and outside the lab. In particular, learning good time management is essential!

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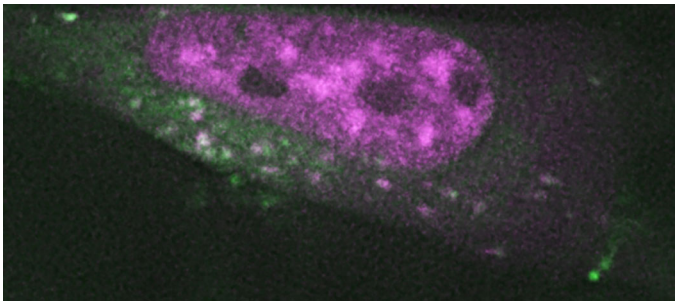

mCherry–SNRPN cytoplasmic structures (purple) co-stain with BODIPY 493 (green), indicating that these structures are lipid-rich, in live SH-SY5Y cells.

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

Particularly for PhD students, a higher stipend would be useful, due to the high living costs in some areas of the UK. For all early-career researchers, more consumables funding for research projects to allow maximum usage of newly developed technologies could improve research output. A longer tenure for research positions would also provide early-career scientists with more stability.

What's next for you?

I will shortly be moving to a postdoctoral position in Prof. Elliot Androphy's lab group at Indiana University to continue investigations into vesicle trafficking and SMN in SMA.

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

I'm a keen hill walker and play cricket for the Staff and Postgraduate team at the University of St Andrews. I also have two house rabbits.

Reference

Thompson, L. W., Morrison, K. D., Shirran, S. L., Groen, E. J. N., Gillingwater, T. H., Botting, C. H. and Sleeman, J. E. (2018). Neurochondrin interacts with the SMN protein suggesting a novel mechanism for spinal muscular atrophy pathology. *J. Cell Sci.* **131**, jcs211482.