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FIRST PERSON

First person – Katherine Fisher

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. Katherine Fisher is the first author on 'A genome-wide RNAi screen identifies MASK as a positive regulator of cytokine receptor stability', published in Journal of Cell Science. Katherine conducted the research in this article while a postdoc with Martin Zeidler at the University of Sheffield, UK. She is now a research associate in the lab of David Strutt, also at the University of Sheffield, investigating mechanisms of coordinated cell polarisation using *Drosophila* genetics and computational modelling.

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

Cells need to receive information from their environment in order to respond appropriately to what is going on around them. For example, they may need to divide more frequently to replace a damaged neighbour. To sense these signals they use proteins on their surface called receptors. The levels and activity of these receptors are carefully controlled, since inappropriate signalling is linked to disease. One such signalling pathway is the JAK/STAT pathway. While, in humans, this pathway is complex with many different components, it is highly simplified in the fruit fly, *Drosophila*. In this paper, we took a whole-genome approach and identified new genes that play a role in regulating the receptor for this pathway in flies. We found that when we disrupt the function of one particular regulator, MASK, we lose receptor levels and signalling capabilities in flies and in human cells. Identification of this new regulator could lead to new therapies against disease.

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

Anyone who has done a genome-wide screen will tell you that they are full of challenges! A technical hitch with a piece of equipment nearly sabotaged half a genome's worth of cells, but the expertise of Steve Brown and the technicians in the Sheffield RNAi Screening Facility helped to save the day.

This paper is the culmination of several years of hard work, and we did find MASK a particularly challenging protein to work with in many ways. All of the authors on this paper contributed to this team effort.

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

I remember feeling a huge sense of relief when I first analysed our triplicate genome RNAi data (after 6 weeks of screening and months of assay development) and realised that our cells were alive and our positive and negative controls had worked! The result that demonstrating that MASK regulates Domeless levels *in vivo* was also particularly exciting, confirming what we had seen in cultured cells.

Katherine Fisher

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

I feel really lucky to have worked with some fantastic people over the years. My first mentor was my PhD supervisor, James Wakefield (now at Exeter). His tirelessly positive attitude was hugely important in getting me through the lulls in results and keeping me motivated.

> **"[…] working across traditional discipline boundaries can be hugely beneficial."**

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 love the investigative nature of science as well as the flexibility and autonomy it brings. I completed my PhD through the Life Science Interface Doctoral Training Centre at the University of Oxford. This instilled a sense that working across traditional discipline boundaries can be hugely beneficial. I now use computational modelling as another tool in my scientific arsenal, which often leads me to think of a problem in a different way.

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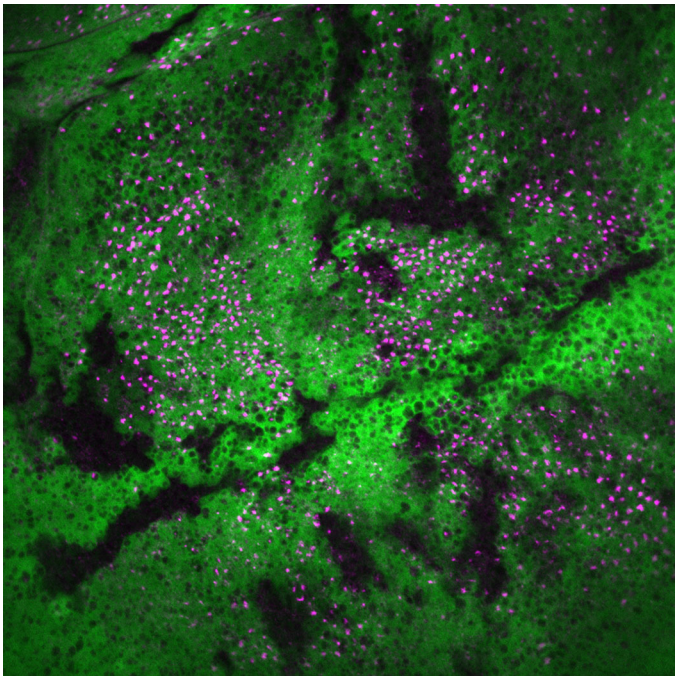

Mutant clones of *mask* (loss of green) have a reduction in Domeless protein (magenta) in *Drosophila*.

What's next for you?

I completed the research for this paper during my postdoc with Martin Zeidler. I am now working in the lab of Prof. David Strutt, still at the University of Sheffield. I continue to be interested in how cells signal to one another to coordinate behaviours, but now I am looking at this in terms of how they coordinate polarity and polarised behaviours.

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

Before I started my PhD, I spent 3 months backpacking around Africa. I went on safari, did a cage dive with sharks and went skydiving!

Reference

Fisher, K. H., Fragiadaki, M., Pugazhendhi, D., Bausek, N., Arredondo, M. A., Thomas, S. J., Brown, S. and Zeidler, M. P. (2018). A genome-wide RNAi screen identifies MASK as a positive regulator of cytokine receptor stability. *J. Cell Sci.* **131**, jcs209551.