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FIRST PERSON

First person – Megan Mc Fie

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. Megan Mc Fie is first author on 'Ciliary proteins specify the cell inflammatory response by tuning NFκB signalling, independently of primary cilia', published in JCS. Megan conducted the research described in this article while a research assistant in Dr Angus Wann's lab at the Kennedy Institute of Rheumatology Research, University of Oxford, UK. She is now a PhD student in the lab of Prof. Martin Knight at Queen Mary University of London, UK, investigating the primary cilium, its structure and associated proteins and the role they play in the regulation of cell signalling.

Megan Mc Fie

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

The primary cilium is a small cell organelle found on most cell types in the human body, often projecting out into the extracellular environment of a cell. Its associated proteins and collective machinery, the 'ciliome', control ciliary structure and function. The cilium has been associated with the regulation of numerous different signalling pathways. We propose that ciliary proteins, such as IFT88, KIF3A, TTBK2 and NPHP4, act outside the ciliary compartment to regulate NFkB signalling and, downstream, specify the cell response to inflammatory cues. This is a novel non-canonical function for ciliary proteins that reveals a potential regulatory axis between cytokine receptors at the membrane and the centrioles at the base of the cilium, which requires further investigation to see whether we could exploit this link in order to tune inflammatory signalling.

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

Trying to study the role of ciliary proteins independently of the ciliary structure is a challenge we faced during this project and is an ongoing challenge for the field. Here, we utilised the macrophage, as it is a cell type that does not typically elaborate a primary cilium but still expresses our protein of interest, IFT88.

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

When we identified that deletion of the protein IFT88, typically studied in the context of the ciliary structure, resulted in an attenuated inflammatory response in bone marrow-derived macrophages, this was a particular moment of reassurance. This strongly supported our proposal for a non-ciliary axoneme role for IFT88, and opens up the potentiality for other 'ciliome' proteins to also have non-cilia associated roles in cellular signalling.

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

We chose the Journal of Cell Science as it captures an audience with a broad scope of interest and is a high-quality journal with a good reputation within the scientific community.

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Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

At this early stage of my career, I am often struck by how lucky I am to have not one or two but many significant mentors that have and continue to offer guidance both in and out of the lab. As essential as the lab-based guidance is, it is the discussions outside of the lab that I am particularly grateful for. For the progress of science and one's own development within research, the academic discussions, sharing of knowledge and training are all essential. In addition to this, I feel particularly fortunate to have been given guidance and insight into what a life in science looks like from a 'real world' point of view. There are many considerations that mentors have highlighted along the way that have made my decision to get on the roller-coaster that is scientific research feel more informed, and have ultimately made the ride that much more enjoyable. A ride I don't hope to end any time soon!

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 have always been curious and have always enjoyed puzzles. I remember as a small child I wanted to open things up and see what was inside. I liked that a collective of small base units of some sort could come together as a whole to perform a function. My dad

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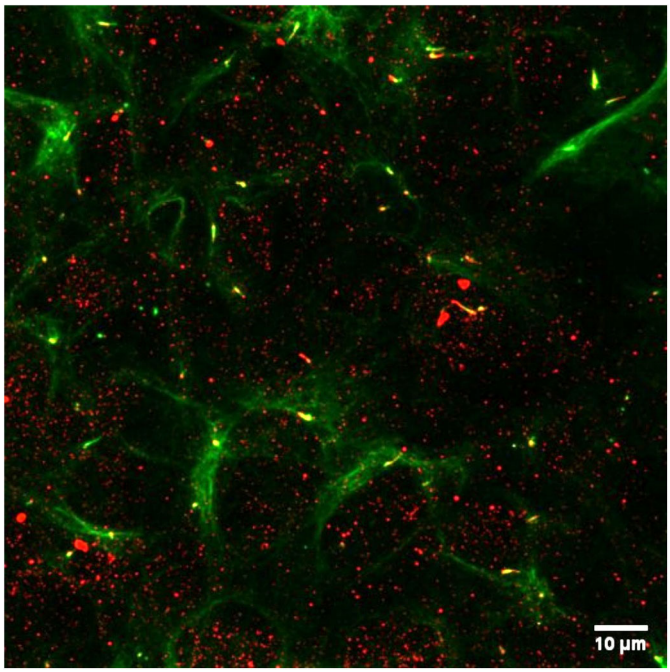

Spot the cilia! IFT88 both inside and outside the ciliary compartment of fibroblast-like chondrocytes. IFT88 in red, acetylated α-tubulin in green.

always had a lot of electrical components and circuit boards lying about, so my interest initially manifested as a fascination with robotics. This morphed into biomedical engineering, and by the time I reached undergraduate studies I had found the biomedical sciences. I think this research field, particularly with its potential for interdisciplinary work, encapsulates and offers a seemingly endless supply of puzzles and things to 'take apart'. It's enjoyable work that hopefully pushes medical treatment options forward and aids the wellbeing of others.

The most interesting moments so far have been witnessing that when things appear to be going wrong, many times this has led to an unforeseen good outcome, often better than the one previously anticipated and planned for.

What's next for you?

I am currently a PhD student, investigating the relationship between the primary cilia structure and the regulation of cell signalling events. Within the next two years I hope to complete my PhD and begin my first postdoc, maybe even working towards a fellowship if all goes well. I will count myself lucky if I can stay in research.

Reference

Mc Fie, M., Koneva, L., Collins, I., Coveney, C. R., Clube, A. M., Chanalaris, A., Vincent, T. L., Bezbradica, J. S., Sansom, S. N. and Wann, A. K. T. (2020). Ciliary proteins specify the cell inflammatory response by tuning NFκB signalling, independently of primary cilia. *J. Cell Sci.* **133**, jcs239871. doi:10.1242/jcs.239871