© 2021. Published by The Company of Biologists Ltd | Journal of Cell Science (2021) 134, jcs259488. doi:10.1242/jcs.259488

FIRST PERSON

First person – Judith Barbara Fülle

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. Judith Barbara Fülle is first author on 'Desmosome dualism – most of the junction is stable, but a plakophilin moiety is persistently dynamic', published in JCS. Judith is a PhD student in the labs of Christoph Ballestrem, David R. Garrod and E. Birgitte Lane at the Wellcome Trust Centre for Cell-Matrix Research, University of Manchester, UK and the Skin Research Institute of Singapore, Agency of Science Technology and Research (A*STAR), Singapore, investigating the nature of cell–cell junctions, in particular the composition and regulation of desmosomes in health and disease.

Judith Barbara Fülle

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

We are multicellular organisms, and our cells have evolved several ways to adhere to each other, which is important because otherwise we would fall apart. In particular, cells in tissues like our skin and heart muscles, which are constantly exposed to stretching, need to 'stick together' and withstand high and continuous mechanical stress. Our study focused on desmosomes, whose name derives from the Greek words *desmós* and *sōma*, meaning 'binding body'. They essentially act like complex force-resistant 'buttons' that hold neighbouring cells together, and others have shown that malfunctioning of desmosomes can lead to severe skin blistering, heart diseases, wound healing defects and cancer progression.

During my PhD, I wanted to study desmosomes in more detail and, following the motto 'seeing is believing', I used fluorescence microscopy to monitor desmosomes and their building blocks (the individual proteins they consist of) in live cells over time. I used fluorescent labels – essentially colouring desmosomal proteins – and saw that these 'buttons' are indeed very stable structures. But I found that one component of desmosomes, named plakophilin 2a (Pkp2a), behaves very differently to the other components. Pkp2a is astonishingly mobile and shuttles within seconds from desmosomes to other parts of the cell and back. We interpret this finding as evidence that desmosomes have two main functions: mediating strong adhesion between cells and acting as a signalling hub. Furthermore, we are interested in how cells are able to get rid of desmosomes when they need to wander more freely, for example when they are closing a wound gap. To study this question, we used a growth factor that triggered the cells we study to change their behaviour from growing in close colonies to migrating away from those colonies. We found that instead of unbuttoning or disassembling desmosomes, one or the other of the neighbouring cells forcefully rips out the whole desmosomal 'button' from their neighbour as it separates from the group. Whilst this finding came as a surprise, it confirms reports that described such internalisation of whole desmosomes by cells in cancerous tissues and at wound edges. These two key findings about the function and turnover of desmosomes help us to better understand and appreciate the importance of desmosomes and are needed in a currently evolving field with high clinical relevance. Finally, as with any scientific endeavour, every answer raises a multitude of new questions, driving the advancement of our knowledge.

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

The project is the result of a wonderful collaboration between Christoph Ballestrem and David Garrod at the University of Manchester in the UK and Birgit Lane at A*STAR in Singapore. My co-author Henri Huppert and I have both spent two years of our PhD projects at each of these labs on opposite sides of the world, separated by an 8 hour time difference. Settling into new environments and adapting to cultural change is exciting but can also be challenging at times, particularly when the labs closed during the pandemic last year. I am very grateful and lucky to have the support of my absolutely brilliant supervisors Christoph Ballestrem, David Garrod, Birgit Lane and Graham Wright, as well as their fantastic teams and friends on both sides of the globe. I would also like to mention the indispensable support I received from my family, friends and fellow PhD students over the past years. I cherish all that I was able to learn from the many discussions during this project, both scientifically and personally.

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

There were a few 'eureka' moments associated with this project, including observing the internalisation of whole desmosomes by cells that are separating in tissue culture and the associated severed keratin filaments. Personally, the most memorable moment was when I first measured the dynamics of Pkp2a. I was at the microscope for a few hours doing FRAP and FLAP on the other desmosomal components, which behave quite similarly and are

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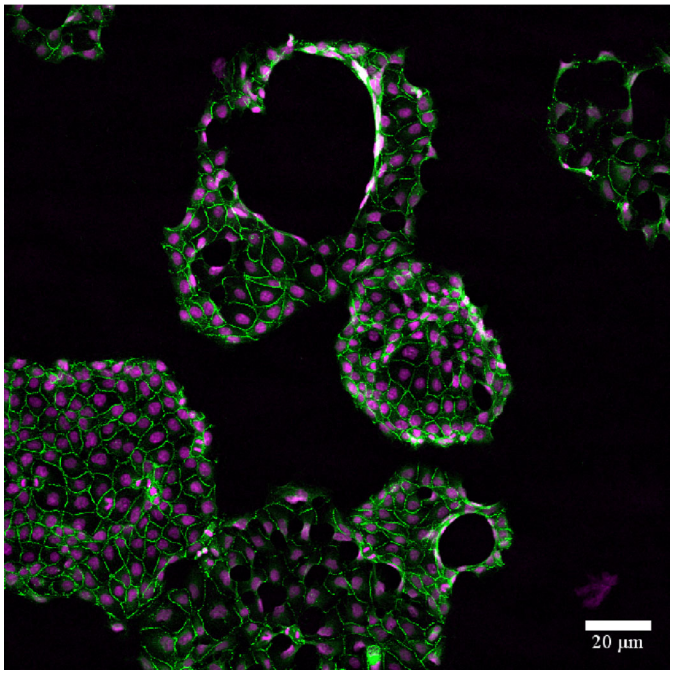

Initial stage of scattering islets of Madin–Darby canine kidney cells treated with 40 ng/ml hepatocyte growth factor. Desmosomes are visualised by immunostaining desmoplakin (green), and cell nuclei are stained with DAPI (magenta).

almost static to the eye. Seeing the fast exchange of fluorescently tagged Pkp2a from and to desmosomes was very exciting and showed me that desmosomes are more than just stable and robust (some may say boring) adhesion junctions – they also function as critically important signalling hubs.

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

Journal of Cell Science is one of my favourite cell biology journals, which reaches both the experts in the field and also the broader community of cell biologists. The paper was handled quickly, and the reviewing process was thorough and very helpful. Additionally, I highly appreciate The Company of Biologists as a publisher, which as a non-profit organisation returns all the profits made from publishing back to the scientists, and I myself have attended several meetings supported by The Company of Biologists.

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 fascinated by nature, and I love understanding and unravelling the complex molecular and cellular relationships in our bodies that are involved in health and disease. I had great science teachers, professors, mentors, friends and family, who inspire me to this day. I studied biology as an undergraduate and worked as a student lab assistant, which made me decide to stay in molecular science. I came to Manchester for the final project of my master's degree and during that time fell in love with microscopy. The opportunity to combine science with getting to know other cultures during my PhD was a stroke of luck. It also showed me how universal the quest for knowledge is, which in the end is the essence of science.

Who are your role models in science? Why?

I don't have any specific role models, but I admire those who create new technologies that enable us to find answers to the many open questions. Isn't it amazing that we can couple mammalian and jellyfish DNA to use GFP to visualise the behaviour of proteins in live cells and organisms, or use CRISPR to deplete specific proteins from cells to explore their function?

What's next for you?

I am currently finishing my PhD and will work in the laboratory of Christoph Ballestrem and David Garrod next summer to hopefully publish some more interesting findings. After being abroad for almost six years, I plan to return to Germany by the end of next year.

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

I enjoy being in the institute late at night and having the microscope entirely to myself.

Reference

Fülle, J. B., Huppert, H., Liebl, D., Liu, J., de Almeida, R.A., Yanes, B., Wright, G. D., Lane, E. B., Garrod, D. R. and Ballestrem, C. (2021). Desmosome dualism – most of the junction is stable, but a plakophilin moiety is persistently dynamic. *J. Cell Sci.* **134**, jcs258906. doi:10.1242/jcs.258906