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FIRST PERSON

First person – Keira L. Rice

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. Keira L. Rice is first author on 'Localized TPC1-mediated Ca^{2+} release from endolysosomes contributes to myoseptal junction development in zebrafish', published in JCS. Keira is a PhD candidate in the lab of Prof. Andrew L. Miller at the Division of Life Science, The Hong Kong University of Science and Technology, Hong Kong, investigating endolysosomal Ca^{2+} signaling in skeletal muscle development.

Keira L. Rice

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

My studies are focused on the zebrafish embryonic equivalent of a tendon (known as the myoseptal junction) and the attachment of slow muscle cells to this region during development. My data suggest that this process requires the activity of two-pore channel type 1 (TPC1) – a protein that has been the subject of my research for the past few years. TPCs are of particular interest to our lab (and many others) because they are an ancient family of cation channels (expressed in sea urchins, zebrafish and humans alike) found on endolysosomes. These are dynamic membrane-bound organelles that act as vehicles to traffic cargo within the cell, or as signalling platforms to regulate a variety of cellular processes. Endolysosomes achieve this, in part, by coordinating the release of Ca^{2+} from their internal stores via various cation channels, including TPCs. These Ca^{2+} signals, as well as the activity of TPCs, are known to orchestrate aspects of differentiation and development. Much work so far (including that of my lab mates) has focused on the roles played by TPC2 – an isoform of TPC1. Therefore, I set out to uncover the possible physiological roles of TPC1 in an intact vertebrate model using zebrafish embryos. I was excited to find that TPC1-decorated endolysosomes are dynamically associated with the myoseptal junction and that TPC1 appears to be involved in the trafficking of key components that anchor skeletal muscle cells to their site of attachment. I have shown that not only do zebrafish embryos with attenuated *tpcn1* expression have a phenotype that is distinct from what has been reported for *tpcn2,* but that they also bear some resemblance to existing zebrafish models of muscular dystrophy.

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

I started to investigate the role of TPC1 in zebrafish slow muscle development for my final year bachelor's thesis project. It was then that I fell in love with imaging and developmental biology. During that year, I tested different antibodies and conducted phenotypic studies on zebrafish embryos between ∼17 and ∼24 hours post fertilization (hpf). I collected some data that pointed me towards the myoseptal junction, but it wasn't until a year and a half into my PhD studies that I decided to immunolabel and image the trunk musculature of several ∼48 hpf embryos. My imaging data from those experiments were striking to me because the slow muscle cell detachments were particularly pronounced against the organized appearance of the skeletal muscle. This was very exciting to me, and I highlighted these findings in my PhD qualifying examination as an aspect of my research on TPC1 that I wanted to investigate further. Since then, I have been motivated to find new ways to test my hypothesis for the role of TPC1 in the development of the myoseptal junction.

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

Journal of Cell Science publishes work that encompasses a broad range of subjects in the field of cell biology and thus it has a wide readership. As we wanted our work on the role of TPC1-mediated Ca^{2+} release from endolysosomes on the formation of the myoseptal junction in zebrafish to be read by people beyond the field of developmental biology, we considered this journal to be a perfect place to submit our manuscript.

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 attribute my decision towards a career in science to my high school biology classes. We had a tight-knit group of just seven students, and our teacher, Mrs McDonnell, would prepare hands-on activities for us every other week. Whether we were soaking an egg in vinegar to learn about osmosis, recreating the 'beads on a string' structure of nucleosomes with wool and cotton, or folding paper to study the secondary structures of proteins, my desk partner and I always had the best time. When it came to selecting a lab for my bachelor's thesis, I approached Prof. Andrew L. Miller because I thoroughly

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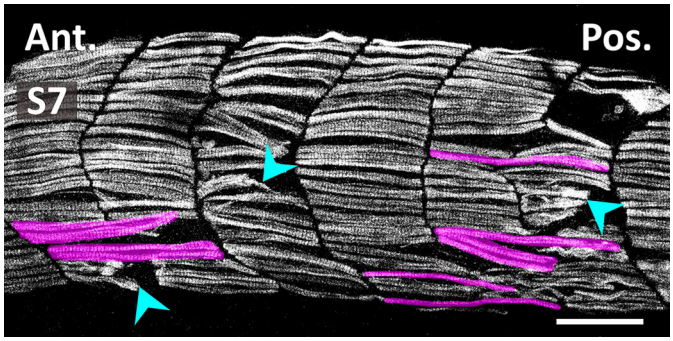

Immunofluorescence image showing the trunk musculature of a ∼48 hpf zebrafish embryo depleted for *tpcn1* and *p53*. The embryos that had been injected with the *tpcn1*-T-MO + *p53*-MO and immunolabelled with a primary antibody to myosin heavy chain (grey). Myofibers that cross the somite boundaries are pseudocoloured in magenta and detached SMCs are indicated by cyan arrowheads. S7, Ant. and Post. are somite 7, anterior and posterior, respectively. Scale bar: 50 µm.

enjoyed his animal physiology classes and I was fascinated by the figures and images he presented of skeletal muscles. To this day, I am mesmerized by how the beautifully striated bio-architecture of muscle cells came to be. During my 'zebrafish-husbandry bootcamp' by our wonderful technician, Ms Mandy Chan, I got to collect and witness zebrafish embryos develop under the stereomicroscope for the first time. That experience was amazing to me. It reminded me of when my brother and I collected tadpoles as children and watched them grow up. When my friends and family ask me why I am studying zebrafish, I wish I could bring them to the lab so they can see for themselves the wonders of developmental biology and how much we can learn from these amazing model organisms.

"To this day, I am mesmerized by how the beautifully striated bio-architecture of muscle cells came to be."

Who are your role models in science? Why?

Dr Elizabeth Blackburn is one of my role models in science. I learned about her work with *Tetrahymena thermophila* and the characterization of telomeres during an undergraduate course. I was fascinated by her discoveries and admired the approaches she took that led her to them. She taught me to let curiosity guide my research, and that you can ask big questions about biological life using unassuming experimental systems (as a freshman, my knowledge of model organisms in science was limited to *Escherichia coli* and mice). Since then, I have been inspired by how her work and lab output has supported the progress of many research directions (in ageing and cancer research, to name just a few).

What's next for you?

Thesis deadlines aside, I am currently searching for my next research adventure. I am not quite sure what that entails just yet (whether it will be another zebrafish tale or not), but I hope that wherever I venture, imaging will be a part of it. Outside the lab, I would also like to gain more experience in scientific communication by continuing to work on scientific blogs and visualizations.

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

In the past year, I started to attend an Irish dancing class. Irish dancing is something I have always wanted to learn since my parents took me to watch Riverdance on tour in Shanghai when I was a child. As the only adult in the class, I am surrounded by talented and energetic youngsters who are very patient when they teach me new moves. I usually return to the lab the day after class with sore legs, but tapping my worries away has helped me through the ups and downs of my PhD.

Reference

Rice, K. L., Webb, S. E. and Miller, A. L. (2022). Localized TPC1-mediated Ca^{2+} release from endolysosomes contributes to myoseptal junction development in zebrafish. *J. Cell Sci.* **135**, jcs259564. doi:10.1242/jcs.259564