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FIRST PERSON

First person – Kelli Fenelon

First Person is a series of interviews with the first authors of a selection of papers published in Biology Open, helping researchers promote themselves alongside their papers. Kelli Fenelon is first author on 'Transgenic force sensors and software to measure force transmission across the mammalian nuclear envelope *in vivo*', published in BiO. Kelli conducted the research described in this article while a PhD Student in Sevan Hopyan's lab at the University of Toronto, Canada. Kelli is now a postdoc in the lab of Theodora Koromila at The University of Texas at Arlington, USA, investigating the intersection of developmental biology and mechanobiology.

Kelli Fenelon

Describe your scientific journey and your current research focus

I obtained two Bachelors in Science in Biochemistry and Mathematics at the University of Idaho before doing my PhD in Molecular Genetics at the University of Toronto in the Hopyan Lab at the Sickkids Research Institute.

I am currently doing a postdoc in the Koromila Lab at the University of Texas at Arlington.

Concurrent with my undergraduate studies, I performed immunological and developmental biology research in *Arabidopsis* and tomato and realized my passion for developmental biology.

I became aware of Sevan's amazing research in forelimb morphogenesis and successfully endeavoured to join his lab. In his lab, through my nuclear mechanotransduction project, I developed expertise in super resolution microscopy, biology of the nucleus, limb bud morphogenesis, and mechanobiology.

I'm currently seeking to carry this experience forward and focus it as I continue to study nuclear dynamics in development using optogenetics in the Koromila Lab.

Who or what inspired you to become a scientist?

From a young age, I've always been interested in questions of natural philosophy and physical inquiry. While I enjoyed and excelled equally in engineering, I ultimately came to consider it an unfulfilling career path for my personality and decided to become a scientist.

Once my mind was made up to make the equations rather than merely use them, so to speak, I swiftly decided the broad question of how complex organs and organisms form is not only fascinating on a fundamental level, but the best way to make the greatest impact with my career.

Despite my somewhat bohemian, solitary character development, I could never have reached this place on my path without the guidance of my undergraduate mentor Dr Zonglie Hong, and my PhD mentor Dr Sevan Hopyan who helped me to understand the realities and potentials of developmental biology.

How would you explain the main finding of your paper?

The mechanical and visual environment of living embryos is extraordinarily messy, creating extreme barriers to precise measurements of the small physical differences between cells of early developing embryos.

This hurdle is inconvenient to early embryonic mechanobiology enquiries because crude methods used for measuring these differences in adult tissues are largely inadequate as the cells of the early embryo are expected to be somewhat uniform in physical properties compared to those of adult tissues, yet even subtle differences during this time of rapid transformation may be of great importance in proper development.

We asked the question of whether differing amounts of relative force is transmitted from different tissues onto the copies of the genome within the nuclei of the cells in those tissues during early embryonic development.

To answer this question, we developed nano-scale molecular tools to measure tension across proteins that link the nuclear membrane to the genomic DNA.

These tools, while having profound potential utility, proved difficult to utilize in the messy background of the living embryo.

In fact, a similar attempt was made in another lab, looking at the cell membrane rather than the nuclear membrane in fly rather than

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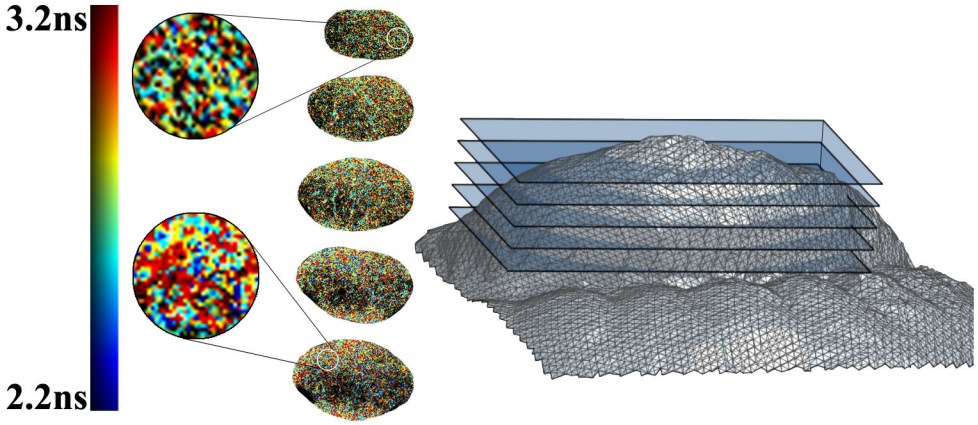

Visualization of a proximodistal forelimb bud tension gradient (tension increases with lifetime) between the nuclear membrane and chromatin (NmpTS).

mouse embryos which concluded with the suggestion that the endeavour was hopeless.

To overcome these hurdles and ultimately show expected tension differences between beating heart cells versus brain cells and somewhat less expected tension differences within the developing mouse arm, we developed a software approach to extract the signal of this type of sensor from the significant noise of living embryonic tissues.

Our work can now be used by other researchers to do further studies with similar sensors and our developmental findings mark the beginnings of a potential understanding of mechanical and gene regulatory interplay.

What are the potential implications of this finding for your field of research?

We developed a valuable software tool, transgenic tension sensors in mice, and revealed a spatiotemporal gradient in subcellular force transmission during forelimb bud morphogenesis.

Our analytical approach to dealing with the challenges of *in vivo* quantitative microscopy provides a methodology to overcome these hurdles which should hold ubiquitous utility for transgenic FRET sensors in most species.

Additionally, our transgenic transnuclear tension sensor mouse lines (NmpTS, NespTS) can be interrogated in most, if not all, tissues of all stages of development and even from adult animals.

Finally, the existence of a potentially evolutionarily derived and/or utilized mechanical transcriptional tool implied by the existence of transnuclear force gradients in developing embryonic tissues presents a foundation for an exciting, nascent avenue of morphogenetic enquiry.

Which part of this research project was the most rewarding?

Spending more than a year engineering, cloning, and generating six transgenic tension sensor mouse lines only to be met with the realization that current analytical tools were inadequate to produce reliable data from them was extraordinarily frustrating. It was, then, immeasurably rewarding when we developed our software package and began comparing measurements taken in heart and brain cells and consistently reproducing the findings of the literature.

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What do you enjoy most about being an early-career researcher?

The clearest advantage to being at this stage, rather than a more advanced one, in my career is that I’m able to collect experiences and knowledge in the lab that will likely be invaluable when I eventually run my own lab that will be impractical to obtain later on.

What piece of advice would you give to the next generation of researchers?

I would advise the next generation of researchers to focus on the research. When choosing a lab from your undergraduate, choose based on your interests rather than school ranking, personality, etc.

What’s next for you?

I am currently in the first year of a postdoc with the Koromila Lab at UTA and I’m continuing to study early embryonic development while gaining expertise in new super resolution microscopy techniques and optogenetics while on my way, I hope, to having my own lab to study transcriptional and mechanobiological interplay in guiding cell differentiation in development.

Reference

Fenelon, K. D., Thomas, E., Samani, M., Zhu, M., Tao, H., Sun, Y., McNeill, H. and Hopyan, S. (2022). Transgenic force sensors and software to measure force transmission across the mammalian nuclear envelope *in vivo*. *Biol. Open.* **11**, bio.059656. doi:10.1242/bio.059656