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FIRST PERSON

First person – Lai Kuan Dionne and Eric Peterman

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. Lai Kuan Dionne and Eric Peterman are co-first authors on 'FYCO1 regulates accumulation of post-mitotic midbodies by mediating LC3-dependent midbody degradation', published in Journal of Cell Science. Lai Kuan Dionne is a post-doctoral associate in the lab of Moe Mahjoub at Washington University School of Medicine, investigating the molecular mechanisms of post-mitotic midbody accumulation and secretion in health and diseases. Eric Peterman is a PhD student in the lab of Rytis Prekeris at the University of Colorado-Anschutz Medical Campus, investigating post-mitotic inheritance and roles of the midbody.

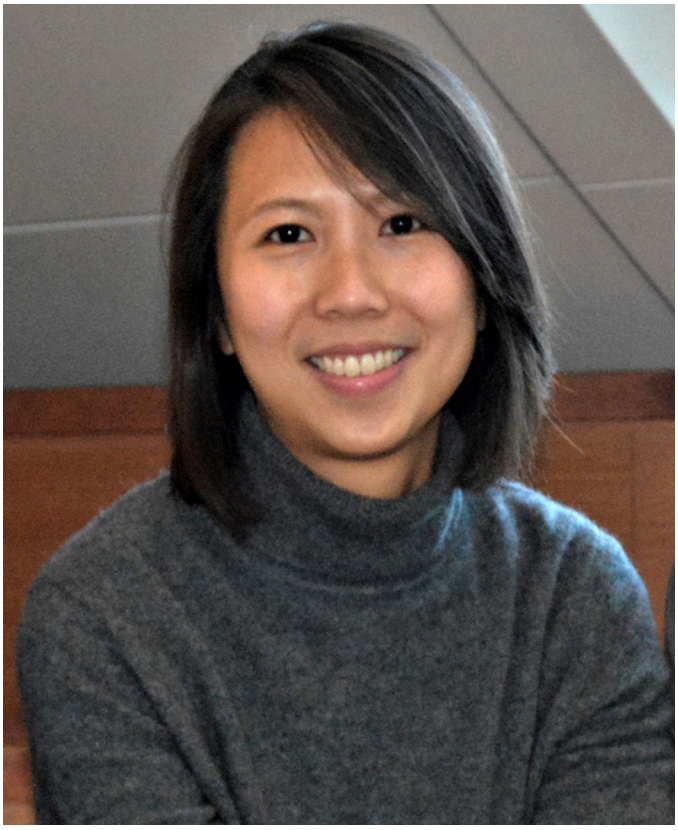
How would you explain the main findings of your paper to non-scientific family and friends?

L.K.D: The midbody is a protein-rich structure that forms during cell division. It is required for the final separation step, where two new daughter cells are generated. After cell division, the midbody is considered as cell debris with no known biological function. However, recent studies have shown that many stem cells and cancer cells accumulate midbodies by avoiding degradation. Understanding the mechanisms of midbody accumulation and degradation has become the focus of intense research. In this study, we showed that cancer stem cells have rampant accumulation of midbodies. We further discovered that a protein generates a limiting membrane surrounding the midbody and targets the midbody for degradation. Interestingly, manipulating the level of this protein not only changes the extent of midbody accumulation in cancer cells, but also the cell's ability to invade its environment.

E.P.: Post-mitotic midbody biology is a relatively new field, in which scientists are exploring the roles of an organelle that was once thought to be 'junk'. The midbody has typically been studied for its role in cell division, and has been thought to be immediately degraded once it has fulfilled this role. Residing between the two daughter cells during division, it recruits proteins necessary for the completion of cell division. However, this new emerging field is finding that the midbody can exist long after division, and can have roles post-mitosis. In this work, we study the role of a protein that is necessary for midbody degradation. Without this protein, we concluded that cells can have altered functions and fates due to midbody accumulation, including their ability to generate tumours and become invasive.

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

L.K.D.: When analysing the accumulation of post-mitotic midbodies in adherent cancer cell lines, we found that the level of accumulation fluctuated quite a bit, possibly due to different 'stem states' of the cells. To overcome this, we decided to sort the cancer stem cells by flow cytometry and cultured the cells as spheroids. By doing this, we were able to better maintain the cell 'stemness', which allowed us to accurately analyse midbody accumulation.



Lai Kuan Dionne

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

L.K.D.: I am fascinated by the fact that only certain populations of post-mitotic midbodies are degraded by FYCO1. Assuming that the process of midbody accumulation occurs slowly over time, it is plausible that only the oldest of the post-mitotic midbodies (with an increased chance of misfolding or aggregation) are being targeted for degradation by autophagy. The question then becomes: what defines the age of these post-mitotic midbodies and how does the cell sense the age of these protein-rich organelles? This is something that I will be interested to pursue in future work.

Have you had any significant mentors, and how have they helped you?

L.K.D.: Throughout my research career, I have been very fortunate to have many wonderful mentors. My advisor, Dr Alexander Sorkin, provided a very conducive learning environment during my thesis years. With Dr Sorkin, any new finding, no matter how exciting, was not celebrated until after many repetitions and confirmation using different approaches. This has provided a very strong foundation for me to do rigorous science. Both my post-doctoral mentors, Drs Rytis

Lai Kuan Dionne's contact details: Washington University School of Medicine, Renal Division, St Louis, MO 63110, USA. Eric Peterman's contact details: University of Colorado-Anschutz Medical Campus, Department of Cell and Developmental Biology, Aurora, CO 80045, USA.
E-mail: dionnel@wustl.edu; eric.peterman@ucdenver.edu

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Eric Peterman

Prekeris and Xiao-Jing Wang, played a pivotal role in nurturing my scientific independence. They allowed me the freedom to pursue my own ideas yet ensured my research directions stayed on track. My current mentor, Dr Moe Mahjoub, has recently transitioned from a post-doctoral researcher to a successful principal investigator. I greatly benefit from our conversations on the trials and tribulations a postdoc must undertake to become a faculty member.

"I would recommend the 'focus–defocus–refocus' approach."

What's the most important piece of advice you would give first-year PhD students?

L.K.D.: I would recommend the 'focus–defocus–refocus' approach: along with good documentation, performing high-quality experiments requires a lot of focus and attention to detail. However, there are times when experiments seem to yield results that do not make sense. Instead of spinning the wheels in troubleshooting, I see this as an opportunity window to 'defocus' from bench work and take a broader view of the entire project. This can be spending time in the library or attending scientific presentations that are associated with your research interest. Through this, you may find new ideas or approaches that will allow you to strategise and then refocus on your project again.

E.P.: I am a fourth-year PhD student and so still have a lot of learning to do, but I have a little wisdom to share with first-year students. My biggest piece of advice would be to pick a mentor who not only performs research that you are interested in, but also has a mentoring style that suits you. If you prefer a hands-off approach, consider completing your PhD in a large lab where you see your mentor once a month. If you think you need an extra boost in your experimental design and approaches, then perhaps a younger mentor or a smaller lab is the best fit for you. Neither is the right or wrong choice, you just need to pick the best choice for you and your lifestyle.

"Pick a mentor who not only performs research that you are interested in, but also has a mentoring style that suits you"

What's next for you?

L.K.D.: I am applying for a Research Career Development Award from NIH, which will centre on the study of midbody biology. For me, getting the award will be a springboard to facilitate my transition from postdoc into a faculty position. I love to teach and I see myself retiring as a university professor.

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

L.K.D.: I have loved music since I was a child. I often find myself more expressive through music than words. Before my PhD training in the USA, I was a hotel lounge pianist in Malaysia. As a graduate student, I could not afford a piano so I volunteered to play the lounge piano for the university hospital on campus. It was a great getaway to collect my thoughts about experiments during incubation time.

Reference

Dionne, L. K., Peterman, E., Schiel, J., Gibieža, P., Arvydas, V., Jimeno, A., Wang, X.-J. and Prekeris, R. (2017). FYCO1 regulates accumulation of post-mitotic midbodies by mediating LC3-dependent midbody degradation. *J. Cell Sci.* **130**, 4051-4062.