

FIRST PERSON

First person – Siyang Han

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. Siyang Han is the first author on 'Substratum stiffness tunes proliferation downstream of Wnt3a in part by regulating integrin-linked kinase and frizzled-1', published in Journal of Cell Science. Siyang is a graduate student in the lab of Celeste Nelson at Princeton University, USA, investigating how biochemical signals and mechanical cues from the cellular microenvironment integrate to regulate cell proliferation, apoptosis and epithelial–mesenchymal transition.

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

Breast tumours are often detected by touch because they are harder than normal breast tissue. In this study, we hoped to understand the transition of cell proliferation, from controlled to uncontrolled, in these stiffer lumps. We found that the growth-promoting factor Wnt3a only induces cell proliferation when the cellular microenvironment is stiff, like in tumours. Soft microenvironments, like normal breast tissue, can protect cells from too much proliferation, even if an excessive amount of Wnt3a is present.

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

At first, handling cells cultured on soft substrata (130 Pa) was difficult for me. It was hard to obtain enough protein samples because the synthetic substratum was too soft to use a cell scraper. Moreover, as cells form multicellular clusters on soft substrata, imaging and immunostaining for protein translocation was also challenging. I overcame these challenges by patiently optimizing the protein extraction protocol and seeking advice from Princeton's confocal imaging facility.

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

Our 'eureka' moment was when we found that the expression of the Wnt receptor frizzled-1 is regulated by substratum stiffness and integrin-linked kinase (ILK). At the time, we were trying to understand how cells respond differently to Wnt3a depending on the stiffness of the microenvironment. We decided to check if any of the frizzled receptors are affected by substratum stiffness. After looking at all the frizzled receptors, I was thrilled to see that stiff substrata increased the expression of frizzled-1. I further found that depleting ILK resulted in a decrease in frizzled-1 levels. These data inspired the molecular mechanism of our study and are the latest example of the crosstalk between Wnt signalling and cellular mechanotransduction.

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

I'm grateful to my advisor Prof. Celeste Nelson, who trusted me enough to give me so much freedom to explore, yet was always



Siyang Han

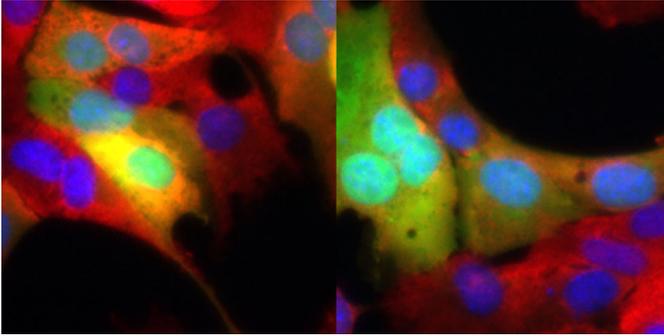
there to steer my project in the right direction. She also instilled in me the importance of the ability to communicate science with audiences of diverse backgrounds by providing feedback at my presentations and supporting me to attend various conferences. I'm also grateful to all the members of the Nelson lab, who share with me not only the most insightful scientific inputs, but also endless fun and joy.

“Try to consider each experimental design, troubleshooting and optimization process as a problem-solving task for yourself.”

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

Stay curious. To me, researching a scientific project is a lot like playing escape room (in slow motion, sadly). Try to consider each experimental design, troubleshooting and optimization process as a problem-solving task for yourself. This helps a lot in stimulating curiosity. Don't drown yourself in the technical obstacles; instead, actively look for clues and exchange ideas with your peers. Once you have a lead, dig deeper. At the same time, keep reminding yourself of the big-picture questions and your motivations from when you first started the project.

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Ectopic expression of integrin-linked kinase (green) led to increased expression of frizzled-1 (red) compared to the expression of GFP only (right).

What changes do you think could improve the professional lives of early-career scientists?

I hope that there will be more resources to support graduate student career development. Graduate school is full of opportunities like conferences, fellowships, workshops and internships. However, this plethora of choices is sometimes overwhelming. In my opinion,

career development requires informed planning years before entering the job market. I believe that more exposure to various career options and more assistance in working out a defined career path would benefit young scientists tremendously.

What's next for you?

I will continue with my current graduate work to study how fluid pressure affects invasive behaviours using a 3D culture model.

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

I have been collecting pencil sharpeners since I was six years old and have been keeping a record (serial number, name, maintenance etc.) for each one of them ever since. I later overheard that this was planned by my mom to nurture me to become an organized person. I'm not entirely sure if the masterplan worked on me, but thanks Mom!

Reference

Han, S., Pang, M.-F. and Nelson, C. M. (2018). Substratum stiffness tunes proliferation downstream of Wnt3a in part by regulating integrin-linked kinase and frizzled-1. *J. Cell Sci.* **131**, jcs210476.