

## FIRST PERSON

# First person – Leyao Shen and Deepika Sharma

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. Leyao Shen and Deepika Sharma are co-first authors on 'Biphasic regulation of glutamine consumption by WNT during osteoblast differentiation', published in JCS. Leyao is a PhD student in the lab of Courtney Karner at Duke University School of Medicine, Durham, NC, United States, investigating the role of amino acid metabolism in osteoblast differentiation during bone development. Deepika is a post-doc in the same lab, who is interested in understanding the role of metabolism during bone formation and maintenance in order to identify novel targets for bone disorders.

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

**L.S. and D.S.:** We are interested in how amino acids affect the maturation and activity of osteoblasts, which are the primary bone-forming cells. Decrease in osteoblast number or their activity leads a common age-associated disease, osteoporosis, which affects millions of people worldwide. Our lab previously identified the amino acid glutamine as a critical regulator of osteoblast maturation. However, it is unknown how glutamine enters osteoblasts. In this paper, we used cell cultures to identify two major glutamine transporters, Slc1a5 and Slc7a7 in osteoblasts. Ablation of either leads to defects in osteoblast differentiation. Slc1a5 and Slc7a7 can serve as novel therapeutic targets to boost osteoblast activity and differentiation to combat osteoporosis.

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

**L.S.:** The recombinant WNT3a we used in the beginning of the study stopped working. We then had to test WNT3a from different companies and finally decided on the one we used in the paper. The next step was a little more exhausting; we repeated all the experiments that we had done before just to confirm the data were consistent with the new WNT3a. From this little obstacle, we truly learned that research is a journey of searching again and again. We are also glad it worked out pretty nicely in the end.

**D.S.:** We observed acute and sustained glutamine uptake in response to osteo-inductive signals (WNT). It was challenging to identify that the uptake was occurring via two different transporters in a biphasic manner with disparate mechanisms, with Slc7a7 regulating the more immediate and Slc1a5 a more sustained response. Additionally, very little literature is available regarding the role of these transporters in osteoblasts.

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

**L.S. and D.S.:** We were first confused how WNT signaling can regulate the expression of the two glutamine transporters with two distinct kinetics. Following revisiting some of our old data and searching the literature, we hypothesized that WNT might regulate



Leyao Shen and Deepika Sharma

this through two different downstream effectors. Canonical WNT- $\beta$ -catenin signals rapidly, regulating Slc7a7. On the other hand, the WNT-mTORC1-ATF4 axis usually produces effects after more than 72 h, which possibly could regulate Slc1a5. Sometimes, re-analyzing old data or just re-reading your old papers may trigger a new idea.

### Sometimes, re-analyzing old data or just re-reading your old papers may trigger a new idea.

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

**L.S.:** When we have journal club in our lab, we always come across papers from Journal of Cell Science, nearly all of which are really high quality. When we looked more into this Journal, we found JCS has a history of nearly two centuries. At that time, we felt it would be an honour to have our work published on JCS. We are glad that we did it!

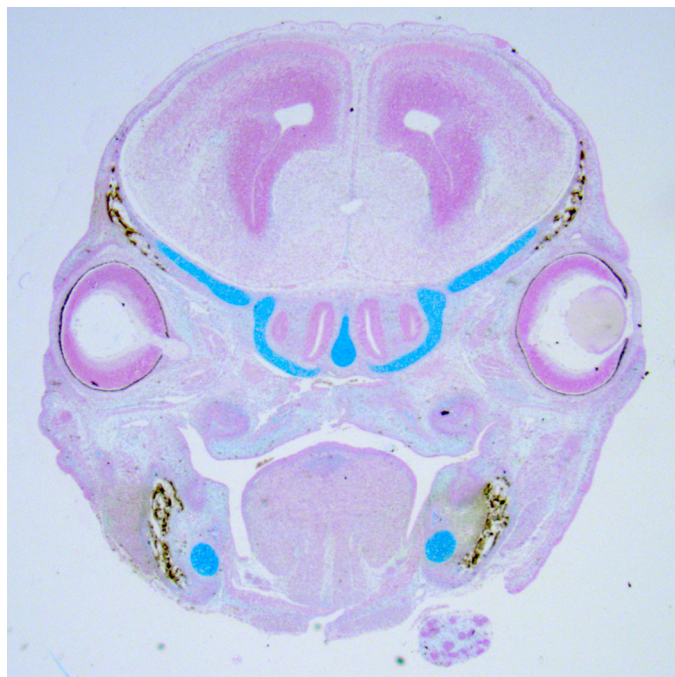
**D.S.:** Journal of Cell Science has a history of publishing papers with novel mechanisms and rigorous science. We believed that our paper represented the quality of work published in the Journal, making it an ideal platform to highlight our work.

### Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

**L.S.:** I personally would like to thank my advisor and PI, Dr Courtney Karner. He is hardworking and has a brilliant mind.

Leyao Shen's and Deepika Sharma's contact details: Duke University School of Medicine DUMC 3710, Durham, NC 27710, USA.

E-mails: leyao.shen@duke.edu; Deepika.sharma@duke.edu



The image shows a cross section of embryonic day 15.5 skull stained with von Kossa (brown) to show mineralized bone matrix and Alcian Blue (blue) to show cartilage matrix.

He helped initiate this project and encouraged us to complete this project. I would say this project would not be here without his ideas and guidance.

**D.S.:** I would also like to acknowledge my PI, Dr Courtney Karner. He was the driving force and motivator for completion of this project. His hard work and attention to detail are very inspiring. He motivates me to achieve higher standards in my work.

I would also like to thank my PhD advisor Dr Matthew Hilton for introducing me to the field of skeletal biology and spiking my interest in the field, as well as being a great mentor and support over the years.

**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?**

**L.S.:** I grew up in a family where my dad used to be a plant chemist and my mother works closely with doctors. This family environment helped me foster an interest in biology from a young age. The first time that I found myself truly passionate about biology was in college at Vassar. I felt fortunate to have been involved in a variety of different projects ranging from biochemistry to developmental biology to genomics, from enzymes to *Drosophila* to coral. This triggered my determination to apply for graduate school and I ended up in the Developmental and Stem Cell Biology program at Duke University, where I met my PhD advisor, Dr Courtney Karner. Now, I am fascinated by the beauty of osteoblasts and bone as a model system.

**D.S.:** I wanted to be a scientist since the first time I saw cells under a microscope in high school in India. This idea was further fostered by all the lab work in undergraduate school and by how much I enjoyed doing an independent study working with sea urchins. I was the only undergraduate to do a podium presentation at the annual sea urchin conference in Woods Hole, MA. This motivated me to attend graduate school at the University of Rochester where I researched and identified a novel role of *Hes1* as an important regulator of digit number. During my PhD, I had the opportunity to complete my work at Duke University. It was at Duke where I met Dr Courtney Karner and was very interested in his work studying the role of amino acid metabolism in bone formation and I decided to pursue my post doc in his lab.

**Who are your role models in science? Why?**

**L.S.:** My role model is the Nobel Prize Laureate Youyou Tu. She is a Chinese scientist who successfully extracted artemisinin, an effective herb-based therapeutic against malaria. I have admired her for long time probably because my father, who was a herb chemist, shared her story with me when I was little. I got inspired by her perseverance, given that the laboratory environment was tough and technologies fell behind in China in the 1960s and 70s. Meanwhile, I really appreciate and cherish the exceptional research environment we have currently.

**D.S.:** My biggest role model is Nobel Laureate Marie Curie. She was the first woman to get a Nobel prize and the only woman to receive it twice. Her commitment and passion for her work is awe inspiring, especially considering the era she was born in.

I am also inspired by Dr A. P. J Abdul Kalam who was not only the 11th president of India but also an exceptional aerospace scientist. He was born into very poor family and overcame all the hardships and achieved great things.

**What's next for you?**

**L.S.:** My next step is to do a year-long postdoc at UT Southwestern. After that, I am planning to go to dental school to apply my knowledge of mineral biology in a more clinical setting.

**D.S.:** My lab is moving to Texas and I have decided to stay back in North Carolina with my family. I plan to take a couple of months off before embarking on my next adventure.

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

**L.S.:** I once travelled in Vienna, Budapest and Prague with no cell phone for 10 days.

**D.S.:** I love to make watercolor art and am an avid baker. I also dabble in poetry.

**Reference**

Shen, L., Sharma, D., Yu, Y., Long, F. and Karner, C. M. (2021). Biphasic regulation of glutamine consumption by WNT during osteoblast differentiation. *J. Cell Sci.* **134**, jcs251645. doi:10.1242/jcs.251645