

FIRST PERSON

First person – Ye Zhang

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. Ye Zhang is the first author on 'Histone H3K27 methylation modulates the dynamics of FANCD2 on chromatin to facilitate NHEJ and genome stability', published in Journal of Cell Science. Ye is a PhD student in the lab of Fang-Lin Sun at Tsinghua University, Beijing, China, investigating epigenetic regulation in DNA repair and carcinogenesis.

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

Histones are the proteins that protect and pack DNA within the cell nucleus. Different kinds of histone modifications can alter the structure and accessibility of DNA, and H3K27me_{2/3} is one of the modifications that makes the DNA more condensed and less accessible. Our work has uncovered a new mechanism through which H3K27me_{2/3} is involved in regulating the repair of DNA double-strand breaks (DSBs), a severe injury of DNA that could lead to cell death or carcinogenesis. We reduced the level of H3K27me_{2/3} by several approaches and in each case found similar inhibition of the repair efficiency of one of the DSB repair pathways. The cells also showed signs of genome instability, a hallmark of cancer. We then discovered the mechanism underlying the inhibition of the DSB repair pathway – altered distribution of a certain protein in cells with reduced H3K27me_{2/3}. When we knocked down production of this protein, efficiency of the DSB repair pathway was restored. These findings provide a new perspective related to understanding cancers with modified H3K27me_{2/3}, which could enlighten the discovery of novel cancer treatment in the future.

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

We started the project over four years ago and I have been working on it ever since. There have been lots of challenges along the road and the biggest one must be the frustration when all the clues seem to be dead ends. I was so lucky to have my husband and my family encouraging me all this time. When I came close to giving up, their encouragement kept me going a little longer and I was always lucky enough to find something to push the project forwards.

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

The ‘eureka’ moment for me was the discovery that FANCD2 binds with H3.1K27M and hypo-H3K27me_{2/3} histones, which is a novel



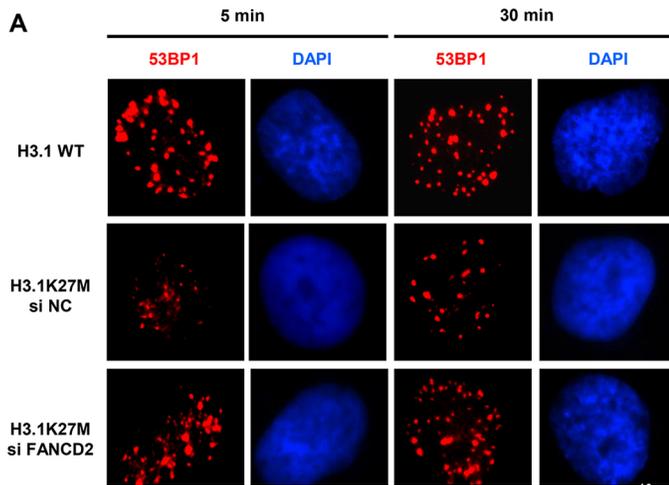
Ye Zhang

finding and also one that came after a long time of getting nowhere. We always thought that the mechanism underlying the inhibition of DSB repair pathway non-homologous end joining (NHEJ) in hypo-H3K27me_{2/3} cells was an altered gene expression profile, as H3K27me_{2/3} is a classic marker for transcriptional repression. I remember that I was so excited to see the mass spectrometry result that showed the increased binding of FANCD2 in hypo-H3K27me_{2/3} mutants, and couldn't wait to verify the results though western blotting.

Have you had any significant mentors who have helped you beyond supervision in the lab?

My PhD supervisor is Prof. Fang-Lin Sun, and I have been in his lab for almost nine years. His great expertise in the field of epigenetics and his scientific rigor have created a favorable environment to complete my thesis project. I appreciate his guidance and mode of instruction a lot, which is to train independent scientists rather than technicians. It has benefited me a great deal and will keep encouraging me in the future. Prof. Sun is also a man with great scientific insight and self-motivation, which sets an admirable example for everyone in the lab.

Ye Zhang's contact details: School of Medicine, Tsinghua University, Beijing 100084, China.
E-mail: zhangye880130@163.com



53BP1, which serves as a marker for DSBs and promotes NHEJ-mediated DSB repair, is shown in red. FANCD2 knockdown rescued 53BP1 foci formation in H3.1K27M cells.

“Try to solve problems on your own first rather than seek help immediately, because in the end all scientific discoveries are new to everyone.”

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

Think independently and trust yourself. Try to solve problems on your own first rather than seek help immediately, because in the end all scientific discoveries are new to everyone.

What’s next for you?

I am now in the final year of my PhD. I love doing research and discovering new things, therefore I would like to pursue a career that offers the fun of research. I realize that there are lots of interesting questions waiting to be answered outside my current research area, so I would like to explore the options more widely.

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

I love cats and I have three in my apartment. Two of them were strays on campus and were only about one month old when I took them home. I am also a marathon runner. When I struggle with tough experiments or am stuck with writing, I go out running for an hour or two and come back to work with a fresh state of mind.

Reference

Zhang, Y., Chang, J.-F., Sun, J., Chen, L., Yang, X.-M., Tang, H.-Y., Jing, Y.-Y., Kang, X., He, Z.-M., Wu, J.-Y. et al. (2018). Histone H3K27 methylation modulates the dynamics of FANCD2 on chromatin to facilitate NHEJ and genome stability. *J. Cell Sci.* **131**, jcs215525.