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FIRST PERSON

First person – Ruiqi Wang

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. Ruiqi Wang is first author on 'Heat resilience in embryonic zebrafish revealed using an *in vivo* stress granule reporter', published in JCS. Ruiqi is an assistant technologist in the lab of Jin Xu at Chinese Academy of Sciences, Shanghai, People's Republic of China, investigating non-invasive ways to cure neurodegenerative disease, and the relationships among circadian, stress granule and neurodegenerative diseases.

Ruiqi Wang

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

When cells are exposed to stresses, many stress granules (SGs) will form in the cytoplasm. Every SG is like a little bunker in the battlefield defending the protein translation process from the invasion of stresses like toxins and virus. Under the microscope, SGs in cells look like oil droplets in your chicken soup and are formed by a process called protein and RNA phase separation. SGs have been intimately linked to stress resistance in cancer cells and the development of some neurodegenerative diseases. Most studies on SGs have been performed in cultured cells or in fixed tissues; therefore, how SGs are regulated in real-time in live animals under stress conditions is entirely unknown due to lack of appropriate tools.

In our study, we added a fluorescent tag to an intact protein (GSBP-1) known to be a good marker for SG in zebrafish using the CRISPR/Cas9 gene editing technique. Through this approach, we could trace the formation of SGs in live zebrafish embryos with a microscope. We have validated that this GFP–G3BP1 reporter could faithfully and robustly respond to some stresses, such as heat shock. We found that SG formation and dynamics differed by brain region in zebrafish. Furthermore, low-heat preconditioning significantly repressed SG formation during heat shock in zebrafish. More interestingly, SG formation is more robust in zebrafish embryos than in larvae and coincided with significant elevated phosphorylated eIF2α and enhanced heat resilience. These were new observations, unlikely to be uncovered without this newly developed tool.

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

There were two major challenges in my project. The first challenge was that it is difficult to fuse the GFP immediately adjacent to either the start or stop codons. We tested many sgRNAs at both terminals. We changed donor from plasmid to linear donor and changed from long homologous arms to short homologous arms. Finally, after numerous attempts, we successfully constructed a SG reporter. The second challenge was that we needed to employ stresses that can induce SG in zebrafish. This part of research is quite interesting because we can ask whether or not physical stresses, such as anxiety, fear or sleep deprivation, can induce SGs. These are questions that have never been exploited due to the lack of an *in vivo* SG reporter. We tested a variety of stress conditions and drugs. While we did not find any physiological stress that were able to induce SGs, we discovered that stresses induced by sodium arsenite, DTT, puromycin, and heat shock can lead to SG formation in GFP–G3BP1 zebrafish. To sum up, keep trying and maintain the passion for research despite the negative results that come every day is my way to overcome these challenges.

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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 came when we found that knock-in of GFP at the immediate N-terminus or C-terminus of G3BP1 was not a viable strategy. Later, we changed the homologous arms to 35 bp in linear donor, as some recent papers suggested, and shifted the knock-in site to the sgRNA cutting site. Finally, we managed to construct our GFP–G3BP1 zebrafish.

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

Journal of Cell Science is a well-respected journal and publishes a wide range of topics relevant to cell biology. I have read many articles in this journal that are related to SGs. We are very glad that our manuscript is published by this high-quality journal.

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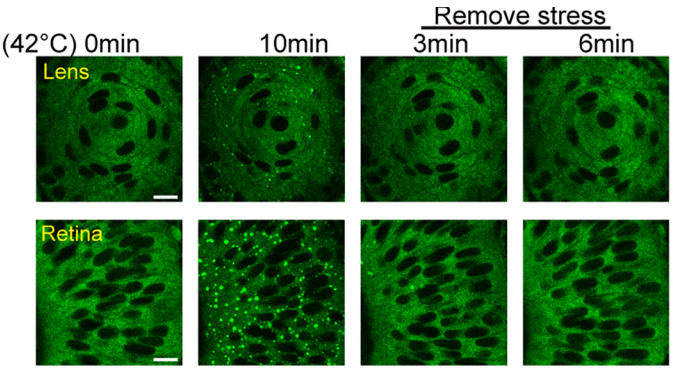

Stress granule assembly and disassembly. Stress granules are detected by an *in vivo* reporter (GFP–G3BP1) in the retina cells of zebrafish during heat shock.

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

Dr Julin Du is the PI of Sensory Integration and Behavior lab at ION. He gave us a lot of suggestions on the paradigms of fear and anxiety in zebrafish. These suggestions helped us better evaluate the stress granules in physiological stress conditions.

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?

Neuroscience is a very exciting field and has a profound influence on our daily life. I remember when I was a high-school student, I was first exposed to neuroscience through science fiction. I was fascinated about the intricacy of our brain, and gradually realized that this field could enable us to find who we are and where we go. Actually, I think neuroscience may start a revolution at both material and spiritual aspects of human life in the future. Another reason I chose to pursue a career in neuroscience is that there are so many diseases caused by neural system dysfunction. One of my family members has schizophrenia, so I can understand that it is very hard for healthy people to accept the strange behaviour of patients and understand their pain. There is no doubt that today there are more and more people suffering from mental diseases and neurodegenerative diseases. This is a very strong motivation for me to study neuroscience. The most interesting moment, and the luckiest moment, is I have had the chance to work in Dr Jin Xu's lab since I graduated from college and started to do research as a staff member. I can say that I have learned a lot in this lab because Dr Xu trained me using the standards for graduate students. This experience hones my research skills and will help me to choose my future research direction.

Who are your role models in science? Why?

My first role model is Eric Kandel because I read his biography "In Search of Memory" when I was a college student. This book not only presents his life as a neuroscientist but also introduced his fantastic work on memory formation with vivid graphs. His book ignited my desire to pursue a career in neuroscience. Another role model is Muming Poo. Dr Poo is a great scientist and has a profound influence on neuroscience development in China. I also admire the work of Li-Huei Tsai and Henrik Ehrsson, both of them have given speeches at ION, and their research approach blows me away. All of these scientists' work and stories inspired and encouraged me to become a neuroscientist.

What's next for you?

After graduating from college, I have been working in Dr Jin Xu's lab as a staff member. These 3 years of work have changed me a lot. I used to keep doubting my ability to do research, but now this hesitation has faded away because of Dr Xu's patient guidance and my accepted work at JCS. Next step for me is to enroll in a PhD programme and get my PhD degree. I'm really looking forward to this.

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

I enjoy running because it is a great way to keep my mind and body healthy and cultivate my perseverance and integrity. Currently, I am preparing for the marathon in our city. In addition, I enjoy watching movies and playing video games.

Reference

Wang, R., Zhang, H., Du, J. and Xu, J. (2019). Heat resilience in embryonic zebrafish revealed using an *in vivo* stress granule reporter. *J. Cell Sci.* **132**, jcs234807. doi:10.1242/jcs.234807