

## FIRST PERSON

# First person – Guan Chen

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Guan Chen is first author on 'Oxidative stress induces chromosomal instability through replication stress in fibroblasts from aged mice', published in JCS. Guan is an Assistant Professor in the lab of Kozo Tanaka at Department of Molecular Oncology, Institute of Development, Aging and Cancer (IDAC), Tohoku University, Sendai, Japan, investigating aging and cancer-related research.

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

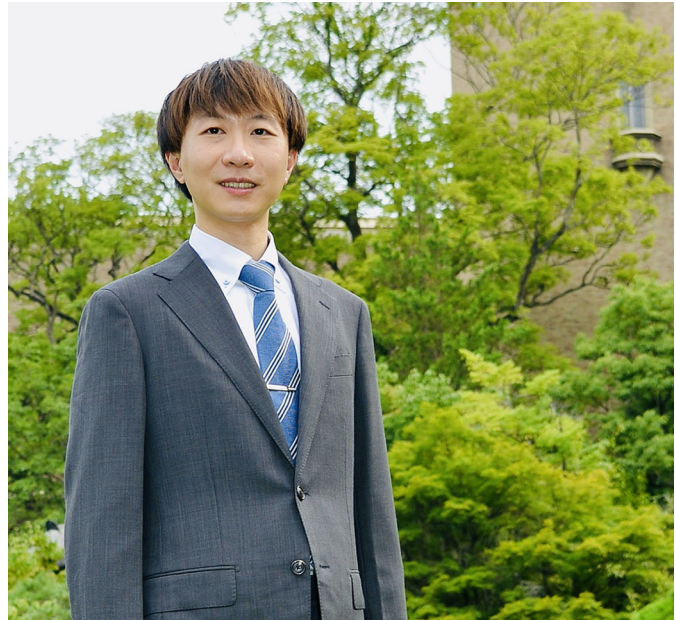
Our paper reports that the number and structure of chromosomes in connective tissue cells called fibroblasts from old mice (24 months old) were increased compared to young mice (2 months old). This is due to chromosomal instability, a condition in which chromosomes are not evenly distributed when cells divide. In the cells of old mice, reactive oxygen species (ROS) were increased, and the addition of antioxidants reduced chromosome mis-segregation, suggesting that oxidative stress is a cause of chromosomal instability. The increase in ROS was thought to be related to mitochondrial dysfunction. Chromosomal instability is known to be caused not only by cell division defects but also by problems with DNA replication. We found that in aged mouse fibroblasts, DNA replication does not proceed smoothly (replication stress) due to oxidative stress, which in turn induces chromosomal instability.

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

One of the challenges for me was figuring out how to establish basic experimental techniques in an environment where no one around me had any experience in aging research, since our laboratory mainly specializes in cancer research. The main concept of my research is to directly observe and analyze how somatic cells divide during aging under conditions similar to those *in vivo*. In order to establish a method for isolating and culturing primary cells, I tried to isolate fibroblasts from old mice, but I could not reproduce good results even when I repeated what was described in previous research papers. I gathered useful information by talking to experts in academic societies involved in aging research. In addition, I carried out a detailed literature review of previous studies and, through trial and error, I continuously improved the experimental conditions and established my own method for isolating and culturing primary fibroblasts.

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

While it was difficult to culture primary fibroblasts from old mice under the commonly used 20% oxygen concentration, it was easier under 3% oxygen, which is closer to *in vivo* conditions. When cell division was observed by live-cell imaging under 20% oxygen, an increase in



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chromosome mis-segregation was observed, suggesting that higher oxygen concentration is detrimental to mitotic progression by causing oxidative stress through an increase in reactive oxygen species (ROS). As chromosome mis-segregation was increased in cells from old mice compared to those from young mice, we thought that it might also be caused by oxidative stress, which turned out to be the case! It is known that cells isolated from old mice show an increased ROS production due to mitochondrial dysfunction, and our findings now link this phenomenon to impaired error-free chromosome segregation.

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

I chose Journal of Cell Science because it has a long history and is a very prestigious journal in the field of cell biology. I often read papers in JCS and I am really honoured that my first paper is published there.

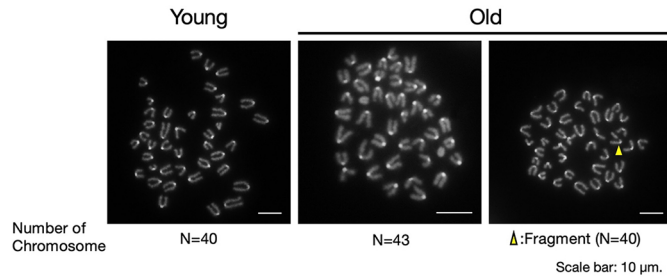
### Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

I really appreciate all the members of the Department of Molecular Oncology, Tohoku University. It is not only through my research, but also through their support that I have finally finished my PhD program.

### 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?

My grandfather was a doctor, and under his influence, I became interested in medicine and life sciences from childhood. Therefore, I entered medical school. While I practiced medicine at a hospital as a resident, I realized the importance of basic research because of the limited effective treatments for elderly patients. Thus, I decided to enter graduate school and engage in research on aging and cancer. As the

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Compared to young mice (2 months old), fibroblasts from old mice (24 months old) show increased abnormalities in chromosome number and structure.

birthrate declines and the population ages rapidly, I will continue to engage in basic research on aging with the goal of realizing a ‘smart aging’ society. I aspire to contribute to the improvement of people’s quality of life through basic research, aiming to solve medical issues in all fields, including aging-related diseases.

**“While I practiced medicine at a hospital as a resident, I realized the importance of basic research because of the limited effective treatments for elderly patients.”**

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

The inspiring role model for me is my supervisor, Professor Kozo Tanaka. Whenever I felt down because of a research deadlock, he always inspired me to cheerfully look for a solution without giving up. That was encouraging to me. He taught me not only how to do experiments, but also how to enjoy scientific research.

### What’s next for you?

Since writing this paper, I have finished my PhD course and I plan to continue to work on aging and cancer-related research, drawing on my experience and research findings.

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

My hobby is music, especially anime and game songs. I sometimes go to Japanese Idol live concerts during my free time.

### Reference

Chen, G., Li, Z., Iemura, K. and Tanaka, K. (2023). Oxidative stress induces chromosomal instability through replication stress in fibroblasts from aged mice. *J. Cell Sci.* **136**, jcs260688. doi:10.1242/jcs.260688