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FIRST PERSON

First person – Kumiko Samejima and Daniel Booth

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. Kumiko Samejima and Daniel Booth are co-first authors on 'Functional analysis after rapid degradation of condensins and 3D-EM reveals chromatin volume is uncoupled from chromosome architecture in mitosis', published in Journal of Cell Science. Kumiko is a post-doctoral fellow in the lab of William C. Earnshaw at the University of Edinburgh, UK, investigating the mechanism of mitotic chromosome assembly and segregation. Daniel is a senior post-doctoral fellow in the lab of Dies Meijer at the University of Edinburgh, UK, and combines basic cell biology with translational medicine to explore the contribution of cell division errors to disease states.

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

KS: Our body is made up of small blocks like Lego blocks, which are called cells. In order to maintain our body, lots of new cells are made every day. Large protein complexes called condensins are required when a cell divides into two daughter cells. We tried to understand what the condensins do during cell division using advanced microscopy techniques. Chromatin in cells carries information about how to make new cells. Chromatin shrinks and changes the shape of the cell every time a cell divides. One of our main findings was that condensin is essential to change the shape of chromatin from spaghetti-like into the shape of two sausages so that it can be delivered into the two daughter cells safely. However, condensin is not required to shrink the chromatin. It is important to understand such basic mechanisms if we want to know why sometimes cells cannot divide properly, resulting in diseases or aging.

DB: The ability of cells to divide (mitosis) is essential for life. The main purpose of mitosis is to separate two copies of each chromosome equally between the daughter cells. Errors in this process can cause cancer and birth defects, with one common example being Down's syndrome. Maintaining the 'normal' structure of a chromosome is key for its functional competence, and this is helped by a number of important proteins, such as condensin, that allow the DNA to condense (hence the name) and occupy a distinctive 'X' morphology. But the whole process of chromosome condensation is not only highly dynamic but it is also hard to monitor and as a result it is poorly understood. In this article, we have not only identified a way to rapidly remove the proteins that hold chromosomes together, but we have also applied a new microscopy method to examine the consequences of this removal.

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Kumiko Samejima

Our overarching goal is to dissect the molecular pathways involved in chromosome condensation, with the hope that this can improve our understanding of why cell division errors occur and how they contribute to the development of disease.

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

KS: It took us a long time to establish SMC2-AID cells to deplete condensin acutely. It was not easy to find out why we couldn't establish a stable cell line. This is because there are so many possible reasons. We did not give up, however, and eventually systematic approaches and a guess based on previous experience helped us.

DB: There were probably two major challenges with this project. (1) The genetic engineering. To generate the required cell lines a lot of work had to go into designing and implementing the cloning strategies. Most of this was performed by Kumiko Samejima (a co-first author) and she did an excellent job. (2) The correlative light electron microscopy (CLEM), which was one of my major contributions to the paper. Our model cell line was the non-adherent DT40 line. These cells make CLEM a nightmare as they all remain round regardless of the cell cycle stage, therefore imaging and re-finding the same cell by light microscopy and then electron microscopy is a challenge. Think of a needle in a haystack…if the hay was actually just other needles.

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

KS: I was really shocked when I first saw, under the microscope, the cells that had condensin acutely depleted. The chromosomes were so ill-shaped that I could not believe that those condensin-depleted cells were in mitosis.

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Daniel Booth

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

DB: I have been fortunate enough to have had numerous mentors during Masters, PhD and post-doctoral studies. I had some very productive years in the lab of Bill Earnshaw, and for the past 12 months I have been gaining some excellent experience working with mouse disease models and transgenics in the lab of Dies Meijer. However, on balance I would say that my PhD supervisors Steve Royle and Ian Prior have been the most influential. Science is an incredibly competitive industry; however, they have consistently and continuously provided help and advice throughout my career so far, and with no obvious benefit to themselves.

"Try to be organised and make every experiment count."

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

KS: You need to know the big picture: what is the biological question of your project? But you should also try to understand the theories behind the individual protocols you use. It helps you to use your time more efficiently.

DB: Try to be organised and make every experiment count. Three or four years is not a lot of time to learn new techniques, completely understand your field, collect and interpret data and finally, publish papers. Therefore maximising the output from every experiment will help to create an efficient labour-to-yield ratio.

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

KS: I went to the 2017 ASCB/EMBO meeting for the first time. I was really amazed to see so much support and so many opportunities for speaking available for each stage of one's career. I wish that I could have had such support. It is important to know when and what we need to focus on at each stage of our career.

DB: Although there are some good sources of funding for scientists making the transition from post-doc to independent researcher, these are limited and incredibly competitive, far more so than 20–30 years ago. This has now evolved to a situation where young scientists with great potential are being forced out of research to find alternative lines of work. At least this is my experience having seen numerous friends and colleagues (reluctantly) head in this direction. Providing more funding opportunities and also a proper incentive for supervisors to assist this transition would really help.

What's next for you?

KS: This is actually a difficult question for me. Project-wise, I have lots of questions and ideas. But I also have to think about my long-term career.

DB: I have just arrived at the six year 'sweet-spot', the stage of a post-doc's career where the jump to independence is often attempted. A majority of the junior group leader fellowships have a seven-year post PhD threshold for applicants, so five to seven years of post-doc experience is apparently a good time to apply. I aim to start applying for these fellowships in the near future and begin my efforts to research independence.

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

KS: I started to run about three and half years ago. Initially I ran 5 km/week, then gradually built up to about 25 km/week. I am really amazed to see how regular exercise can transform a human physically and mentally in a positive manner.

DB: I was a competitive amateur boxer for nearly 10 years, but this was about 10–15 kgs ago! I quit once I had been awarded a Wellcome Trust PhD scholarship. Turning up to the professor's office with a black-eye on a Monday morning just didn't seem appropriate.

Reference

Samejima, K., Booth, D. G., Ogawa, H., Paulson, J. R., Xie, L., Watson, C. A., Platani, M., Kanemaki, M. T. and Earnshaw, W. C. (2018). Functional analysis after rapid degradation of condensins and 3D-EM reveals chromatin volume is uncoupled from chromosome architecture in mitosis. *J. Cell Sci.* **131**, jcs210187.