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FIRST PERSON

First person – Nuno Martins, Fernanda Cisneros-Soberanis and Elisa Pesenti

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. Nuno Martins, Fernanda Cisneros-Soberani and Elisa Pesenti are co-first authors on 'H3K9me3 maintenance on a human artificial chromosome is required for segregation but not centromere epigenetic memory', published in JCS. Nuno conducted the research described in this article while a PhD student in William C. Earnshaw's lab at the Wellcome Trust Centre for Cell Biology, University of Edinburgh, UK. He is now a postdoc in the lab of Ting Wu at Harvard Medical School, Boston, USA, where his research interests lie in the structural and dynamic chromatin regulation of the more mysterious regions of the cell nucleus, such as centromeres, repetitive elements and nucleoli. Fernanda conducted the research described in this article while a postdoc in William C. Earnshaw's lab. She is now an Investigadora en Ciencias Médicas in the lab of Luis Alonso Herrera at Instituto Nacional de Cancerología, México City, México, investigating the transcriptional regulation of microRNAs in breast cancer. Elisa is a postdoc/lab manager in the lab of William C. Earnshaw and is interested in developing human artificial chromosomes (HACs) by applying molecular and synthetic biology techniques to study chromosome segregation and epigenetics in human cells.

Elisa Pesenti (left), Nuno Martins (middle) and Fernanda Cisneros-Soberanis (right)

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

N.M.: Our work tries to understand better some of the most mysterious parts of our chromosomes: they are like a 'jungle' of DNA, sometimes called 'junk' DNA because they are almost never read by the cell, and we don't understand well what their purpose is. These regions form the center of the 'X' shape of chromosomes, and allow them to be pulled to separate away from each other as a cell divides, so each cell has their own copy of the DNA. The small area in the 'jungle' that gets pulled on is a special structure called the centromere, and we still don't know why most organisms have centromeres located in these jungles.

Our work, which manipulated an artificial chromosome inserted in human cells (so the cell's normal chromosomes could survive this process), showed that the centromere remains in place and still works, even when the mechanisms that regulate the jungle are picked apart. But the centromere becomes very unstable, and chromosomes are no longer getting properly separated: this interference can potentially lead to cancer.

We found the jungle and the centromere could recover if we removed our manipulation, showing that the system can resist temporary shocks to these chromosome systems, perhaps from hazardous chemicals and some forms of radiation.

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E.P.: The usage of human artificial chromosomes (HACs) to study chromosomes is quite revolutionary and well exploited by scientists: they are mini-chromosomes, which are able to self-create multiple copies of themselves and be partitioned properly in daughter cells, just as normal chromosomes do. I expect there will be many more applications for HACs in the future.

"Science is never about obvious findings, and in this work, the power of teamwork was essential"

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

N.M.: This project was one developed during the latter half of my PhD, and taught me very impactfully a lesson known by every experienced researcher: missing the characterization of one small phenotypic detail, at the beginning, has the power to later on affect the entire interpretation of your data for the rest of the project. Catching these details as early as possible is always a must. Many an email was exchanged to tease out what the data was telling us. The road to publication was long, with many re-writings as I moved on to my postdoc position across the ocean, but thanks to my co-authors' key experiments, insight from reviewers and many difficult conversations, we were able to tease out what the data had to show us.

F.C.-S.: I think that the main challenge was communication; Elisa and I took on this project after Nuno left the lab. We had difficult conversations (having our collaborator on the other side of the Atlantic is tough) and a lot of discussion about how to structure the paper. I'm glad that technology helped us with this problem, and we could work together as a team.

E.P.: As Nuno said, we would have never achieved such an important result without good communication, honest discussions and open minds. Science is never about obvious findings, and in this work the power of teamwork was essential.

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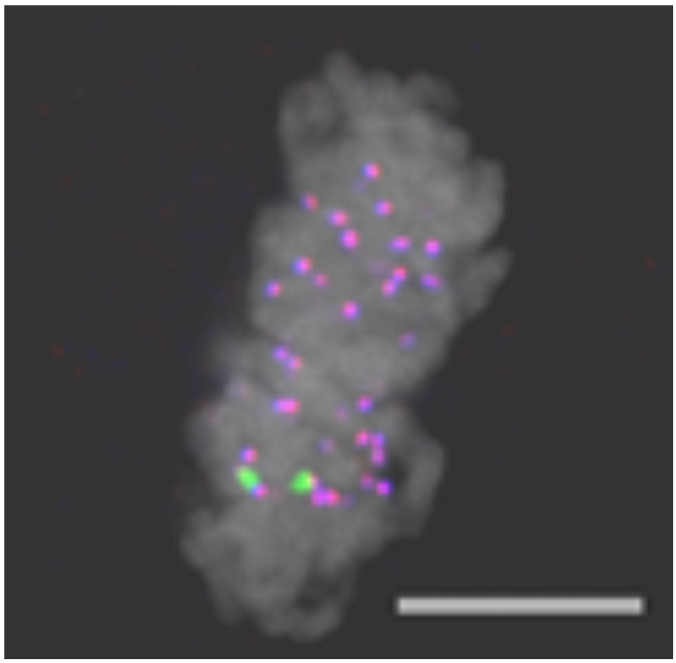

Artificial chromosome (green) and other chromosomes (grey) aligned at the metaphase plate. Centromere proteins CENP-C and Hec1 are highlighted in blue and magenta, respectively. Scale bar: 5 µm.

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

N.M.: I've always seen the JCS as a place where nitty-gritty science is published, which is the way I like it: the important details, the strange curiosities. Hard work on topics that may not be the top trends, but whose data allow a much more solid base for more science to be built upon (especially hidden in supplemental information). Very much like our own work was built on.

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

F.C.-S.: I'm really lucky to have great mentors involved in my career. At university, I had several teachers who gave amazing lectures in cellular and molecular biology and awoke my curiosity in these fields. However, it's always good to have someone in good and bad moments, like my supervisor. The path is not always going to be smooth and nice, and you will need someone to support you and guide you.

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?

F.C.-S.: Curiosity. In my first lab, my mentor told me "Science is a game for kids played by adults". The idea of asking questions and finding the way to answer them motivated me to be a scientist. This work never ends!

E.P.: I decided very early on I wanted to be a scientist and the reason behind this choice was that I wanted to learn more and more about the life sciences, and unveil hidden phenomena that have no explanation. Very ambitious…and naive! Being a scientist taught me that there are many moments of discomfort and uncertainty, but it is behind closed doors that you will find novel answers.

Who are your role models in science? Why?

N.M.: I think it is important not to take others as role models, but to see those more knowledgeable than ourselves as big brothers and sisters, whoever they may be, and from whom we can learn. A single person is not always going to be right, and have all the answers, and that is alright; there is still a lot we can learn from them without unquestioningly believing in them.

F.C.-S.: Definitely, Marie Curie when I was younger, I loved to read everything about her. But now, Alexandra Elbakyan because I consider that science must be accessible to everyone, including people who work at institutions that can't afford to pay for journal subscriptions.

E.P.: I don't believe in blindly following role models, but once an experienced scientist quoted a sentence which has stuck in my mind: "Success is going from failure to failure without losing your enthusiasm".

What's next for you?

N.M.: I will keep doing what I do best and am happy at, which is being a professional scientist: managing my projects, performing experiments, assessing the literature and mentoring other scientists. The demands of group leader careers are, in my opinion, not what they used to be, and present too many constraints to one's ability to do science on a daily basis. I will be exploring the path of a senior scientist wherever it will lead me.

F.C.-S.: I will continue doing science, definitely. But I also would like to focus on two things: (1) engaging people in science and (2) encouraging investment in science. This is important for the future.

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

N.M.: I have learned more about organization, concise and accessible writing, and people management from my hobbies than from fellow scientists or supervisors. Often scientists have difficulty in expressing why certain conventions are done in certain ways, and are often focused on career pragmatisms rather than accessibility and efficiency of their work.

F.C.-S.: I love travelling and enjoying nature. There is nothing more rewarding than climbing a hill and enjoying the view and silence. However, during the COVID-19 times, I have discovered that you can have good fun baking, maybe because there is a little bit of microbiology.

E.P.: I believe doing science is like cooking (and as an Italian this is a very strong sentence to state!): you have to know the basics, you must value the importance of protocols or recipes and then you must apply your judgment and creativity in order to create something unique.

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

N.M.: There should be more orientation, and forward planning, on the part of universities, to channel life scientists to non-academic paths, even non-scientific ones: people with PhDs are highly competent, objective problem solvers and decision makers, which is valuable in many fields. Such links can potentially bring collaborations and investments later on. This would relieve the pressure for PI level positions.

Further, there should be a recognition that senior postdocs, or staff scientists, are not only valuable assets for a lab to hire and keep (and pay for), but that this can be a career path in itself, and arguably is where most of the deep know-how in science is retained.

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They would also be more scientifically independent, as their skills are more important than their publication record, and thus better suited to act objectively.

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

N.M.: That listening and doubting are equally important. Not only figuring how to spot good mentors, reaching out and being humble when learning, but also to practice constant questioning. Of our own ideas first and foremost. To do science is to fall in love with the process of deconstructing ideas and sketching out ways to test them, not of loving ideas and concepts for their own sake.

Learning not to expect help, but also to go seek it. Also to be brave, but speak softly: to do the right thing but pick battles. And having data to back up your claims makes any discussion that much easier.

F.C.-S.: Science is a tough path but really rewarding. Never give up! Ask all the questions that you want but remember to follow the global story. Good luck and enjoy it!

E.P.: Never lose your enthusiasm in science. It is going to be a tough path; there will be falls and moments of demotivation, but only by going through some struggles will you make something meaningful. In your own way.

Reference

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