© 2020. Published by The Company of Biologists Ltd | Journal of Cell Science (2020) 133, jcs249029. doi:10.1242/jcs.249029

FIRST PERSON

First person – Isabella Guardamagna

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. Isabella Guardamagna is first author on 'A functional *in vitro* cell-free system for studying DNA repair in isolated nuclei', published in JCS. Isabella conducted the research described in this article while a PhD student in Lucia Anna Stivala's lab at the Immunology and General Pathology Unit, University of Pavia, Italy. She is now a postdoc in the lab of Andrea Ottolenghi, part of the Radiation Biophysics and Radiobiology group at the University of Pavia, Italy, investigating how cancer cells that are resistant to chemotherapy and radiotherapy acquire proliferative advantages in relation to DNA repair mechanisms and cell-cycle perturbation.

Isabella Guardamagna

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

DNA is continually exposed to agents that are potential causes of several pathological processes; for this reason, cells have evolved a great number of mechanisms to control and repair DNA lesions. Over the years, many laboratory assays using *in vitro* cell cultures were developed to study the DNA repair machinery, but most often the conditions in which this is done are far from how things really are in human cells. We were already familiar with a previous laboratory assay, originally developed to study DNA replication, that makes use of nuclei isolated from cells, but which are still perfectly intact and functioning. In this paper, we further developed this assay and showed that it can be used to study DNA repair when nuclei are isolated from human cells that have been damaged with different agents. In summary, we provide our colleagues with a new technique that can be exploited to better understand DNA repair!

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

The most challenging issue was dealing with recombinant human proteins. Using nuclei isolated from human cells, the amount of endogenous proteins present made it difficult to evaluate the effect of exogenous proteins on the efficiency of DNA repair synthesis. However, by determining the endogenous levels of protein expression in different cell lines, we were able to highlight the *in vitro* activity of recombinant wild-type or mutated human proteins in the cell-free assay.

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

My 'eureka' moment came when we realized that nuclei isolated from human cells exposed to a variety of damage agents responded in the *in vitro* repair assay! We then understood how extremely versatile this technique is for the study of different repair mechanisms. Indeed, I am currently trying to optimize the experimental protocol to continue the study of effects induced by ionizing radiation.

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

We were enthusiastic about the idea of publishing our work in JCS, not only because it is a high-level scientific journal, but because it is the journal where Torsten Krude published his works. Torsten is the 'scientific father' of the replication assay, from which we have developed our new protocol to study DNA repair neo-synthesis, so we can say that his work has made ours possible, and they both now appear in the same journal!

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

I feel very grateful to have had Prof. Stivala as my scientific supervisor and I also want to thank Dr Cazzalini, Dr Perucca and Dr Savio who supported me since my first day in lab. And thanks to Dr Bassi for sharing the lab and three years of PhD.

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?

The reason that led me to pursue a career in the world of science was above all curiosity, and then the idea that even small contributions

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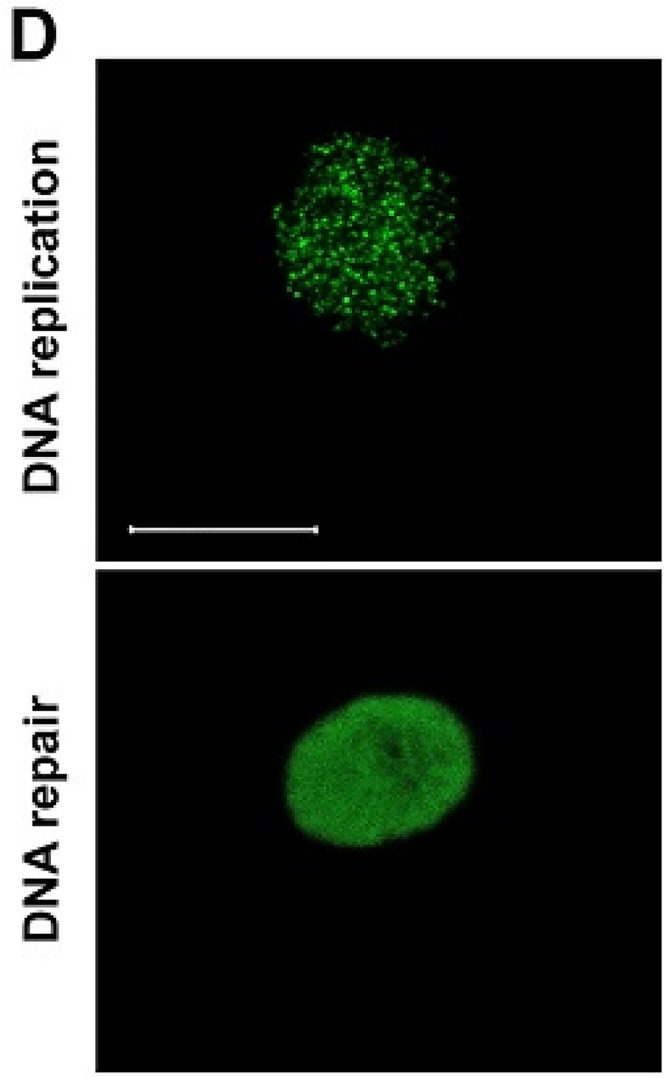

***In vitro* biotin-d UTP incorporation in isolated G1 nuclei from HaCaT cells.** High magnification image of DNA replicative and repair patterns. Scale bar: 10 µm.

could make a difference and lead to small 'revolutions'. See the example of this work; I think that the validation of this new cell-free technique could lead to significant advancements in the understanding of DNA repair mechanisms! This is what motivated me to continue with determination on the path I had started. In general, I think a rewarding career in science always demands determination, perseverance and passion.

Who are your role models in science? Why?

I've always considered as role models all those who carry on their job in science with passion and without considering it a duty. We could say that those who work for passion do not actually work, they have fun!

What's next for you?

Yesterday is history and tomorrow is a mystery, isn't it?

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

I find cooking extremely relaxing. I spend hours and hours in the kitchen (when I have enough time). I also have a great passion for dogs, and – as in the best cinema clichés – thanks to my Border Collie Brenda, I fell in love with my fiancé!

Reference

Guardamagna, I., Bassi, E., Savio, M., Perucca, P., Cazzalini, O., Prosperi, E. and Stivala, L. A. (2020). A functional *in vitro* cell-free system for studying DNA repair in isolated nuclei. *J. Cell Sci.* **133**, jcs240010. doi:10.1242/jcs.240010