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FIRST PERSON

First person – Calin Dragoi

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. Calin Dragoi is first author on 'The oscillation of mitotic kinase governs cell cycle latches in mammalian cells', published in JCS. Calin is a DPhil student in Biochemistry in the lab of Prof. Bela Novak at University of Oxford, Oxford, UK, using mathematical modelling to investigate the emergence of cell cycle properties.

Calin Dragoi

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

The cell cycle is a series of tightly coordinated molecular processes necessary for the proliferation of eukaryotic cells. The main cell cycle events are genome replication during S-phase of the cycle and the equal partitioning of chromatids between the daughter cells in mitosis. The strict alternation of these processes is essential for the viability of cells over many generations. Nevertheless, cells can be experimentally perturbed such that either replicative or mitotic events occur repeatedly, leading to endoreplication or Cdc20 endocycles, respectively, in which the genome is replicated without cell division occurring. To understand how this is possible, we constructed a cell cycle model based on known biochemical interactions and have shown that these 'abridged' cell cycle variants can be reproduced in computer simulations. This has allowed us to propose a mechanism by which the alternation of DNA replication and mitosis is ensured. Subsequently, we confirmed these predictions in the non-transformed cell line, RPE1.

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

For me, a particularly memorable 'eureka' moment came with analysing the transition between wild-type mitotic cycles and Cdc20 endocycles. The insight came from a plot of the oscillation amplitude of APC/C:Cdh1 (which targets cyclins A and B for degradation during G1) with respect to the fraction of active Wee1 (a tyrosine kinase which inhibits CycB:CDK1 during G2; Fig. 5B in the manuscript). The plot showed that when Wee1 is inhibited beyond a specific threshold, the cell very abruptly transitions to Cdc20 endocycles. The nature of this dynamical transition led me to speculate that endocycles can be explained if replication and division are each regulated by potentially autonomous oscillatory modules. I hope to explore this finding theoretically in future work.

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

Journal of Cell Science is a reputable journal where many important contributions to the cell cycle field have been published. Indeed, we felt that submitting our current work here would be a good way to celebrate the 30th anniversary of a previous cell cycle modelling paper published by JCS (Novak and Tyson, 1993), where maturation promoting factor (MPF) regulation was modelled to explain *Xenopus* oocyte mitotic dynamics.

Calin Dragoi's contact details: Department of Biochemistry, University of Oxford, S Parks Rd, Oxford OX1 3QU, UK.
E-mail: calin-mihai.dragoi@trinity.ox.ac.uk

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

My research supervisor, Prof. Bela Novak, has taught me everything I know about cell cycle modelling and has supported me in working on my own research questions and in my pursuit of undergraduate teaching. Our co-author Dr Alexis Barr and her research group have provided invaluable help with experimentally testing our predictions. Further, she has provided many other opportunities for me to apply my mathematical modelling approaches to experimental problems.

In addition, I have many friends and colleagues whose academic experience has helped me navigate the ups and downs of my PhD, chart out the next steps of my career and help me make my work more accessible to a general audience.

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?

Growing up, I was interested in a wide range of subjects, from art and philosophy to the physical sciences and mathematics. This made it challenging to choose a single subject to study at university, but I decided that a degree that would allow me to pursue scientific research after graduation would give me the opportunity to keep learning indefinitely. Eventually, I chose to study biochemistry thanks to the breadth of knowledge from which it draws, from fields from mathematics to evolutionary biology.

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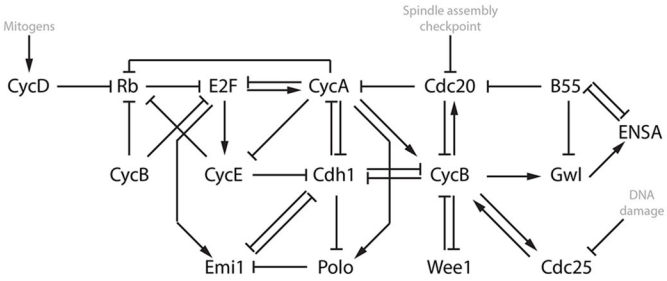

Influence diagram of a subset of the mammalian cell cycle control network. The interactions shown are sufficient to reproduce endoreplication and Cdc20 endocycles in response to CDK1 and Wee1 inhibition, respectively.

One of the most interesting moments of my undergraduate degree was learning that signalling pathways may encode information not just in the biochemical identity of second messengers, but in their temporal and spatial dynamics too. Hoping to understand these surprising phenomena, I decided to study systems biology. During my final-year undergraduate research project, I had the opportunity to learn about the control of cell cycle dynamics under Bela Novak's supervision. My desire to continue this work led me to pursue my doctoral degree.

Who are your role models in science? Why?

My intellectual role models are those who shed light on scientific problems by finding new and insightful ways to frame known facts. Some examples include but are by no means limited to Nicolaus Copernicus and Charles Darwin.

What's next for you?

I am currently in the process of searching and applying for postdoctoral positions. I hope I can find a position that will allow me to continue to use the modelling approaches I have learned during my PhD, engage in experimental collaborations and carry out undergraduate teaching.

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

When I am not doing research or teaching, I greatly enjoy going to the opera. I find the combination of musical, dramatic and visual arts to be remarkably compelling. I am particularly interested in 20th century opera, because the music is enthrallingly original and the plots often explore the inner psychological experiences of the characters.

References

Dragoi, C.-M., Kaur, E., Barr, A. R., Tyson, J. J. and Novák, B. (2024). The oscillation of mitotic kinase governs cell cycle latches in mammalian cells. *J. Cell Sci.* **137**, jcs261364. doi:10.1242/jcs.261364