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FIRST PERSON

First person – Ralitza Staneva

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. Ralitza Staneva is first author on 'Cancer cells in the tumor core exhibit spatially coordinated migration patterns', published in JCS. Ralitza is a postdoc in the lab of Danijela Matic Vignjevic at the Institut Curie, Paris, France, investigating the cell and developmental biology of cell–cell and cell–matrix interactions.

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

My study focuses on colorectal cancer, which is the third most common cancer in human patients worldwide. The main cause of cancer-associated mortality is the metastatic escape of cells, where cancer cells colonize distant organs. To do so, cells need to first acquire the ability to migrate. In order to study cancer cell migration, we chose to work on a mouse model that closely resembles human disease. In this genetic mouse model, mice develop tumors in the intestine that spontaneously metastasize to the lymph nodes, liver and lung. These tumors are composed of a so-called 'invasive front', where cancer cells invade and migrate into the stroma of the tissue, and a tumor core – a deep region previously considered to be a pool of differentiated and immobile cancer cells. In this study, we wanted to address whether cancer cells in the tumor core are immobile or whether they migrate, and, if they do, what are the properties and mechanisms of their migration. To answer these questions, I performed live imaging of tumor samples over long periods of time. I found that cancer cells in the tumor core are migratory, and that their migration is not random. Indeed, cells in proximity migrate in the same direction, suggesting a level of coordination between cells that is dependent on the actin cytoskeleton. This study has implications for understanding human disease, because it suggests that cancer cells might acquire a migratory phenotype before reaching the invasive front, and thus that they are potentially able to metastasize from within deep regions of the tumor core.

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

In order to determine whether cancer cells in the tumor core were motile, I needed to follow the dynamics of the tumor core for long periods of time, up to several days. Therefore, I developed an imaging pipeline to follow tumor core regions in live tissues coming from the mouse, called tissue explants. I encountered challenges related to tissue stability and viability that I overcame by adapting the level of oxygenation of the tissue and with the methodology of tissue mounting. Another type of challenge was inherent to our mouse model, as the development of tumors can take up to a year. This forced us to anticipate what animals we needed a year in advance, so I sometimes faced periods without new samples, leading to difficulties in generating new data.

Ralitza Staneva's contact details: Institut Curie, PSL Research University, 75005 Paris, France.
E-mail: ralitza.staneva@curie.fr

Ralitza Staneva

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

One of my most striking 'eureka' moments came at the microscope when I was trying to enhance the viability of my live tissues. Arriving at the microscope after an overnight acquisition is always a moment of excitement and dread, and I was struck with amazement when I realized that these little pieces of tissue could still be alive and migrating for up to 3 days under the microscope – a non-natural environment for them. Biological processes were ongoing, almost unperturbed, and tissues were alive, even when separated from their mother organism. This made me realize with awe the robustness of the biological phenomenon I was studying.

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

I chose Journal of Cell Science because this journal is known for publishing solid and varied work in cell biology, a field that I particularly appreciate. Because of the diverse and broad readership of JCS, I believe that my work will equally reach cell biologists, cancer biologists interested in live imaging of tumors and biophysicists interested in more quantitative approaches to living tissues. By choosing JCS, I also wanted to acknowledge The Company of Biologists for their valuable support of a more open biological community.

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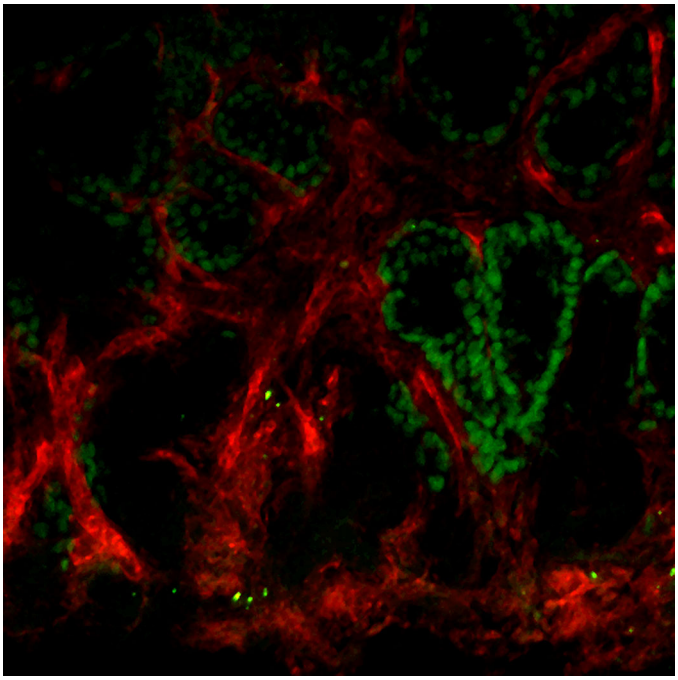

Cancer cells on the move in intestinal tumors in mice. Cancer cells are represented in green (nuclear GFP); stromal cells are in red (membrane Tomato).

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

I strongly believe that one's path in research is largely built upon encounters with people that naturally become mentors through their caring support and advice. For me, such mentors have been senior postdocs in the lab and in my institute who have helped me to navigate through research and its periods of frustrations. My thesis committee has also played a crucial role by supporting my work with kind guidance. Yearly meetings have helped me to better frame my project and the direction it was taking. In particular, my thesis committee supported the project that is now being published in JCS; they believed in it very early on and have encouraged me throughout. Furthermore, I am immensely grateful for enthusiastic discussions about science, about what it takes to be a scientist, and how to navigate the meandering ways of research.

"…the Lindau Nobel Laureate meeting… was a game changer for me…"

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?

I grew up in a family of scientists, where discussions about life sciences were common and fueled my curiosity. A very striking moment of my career was when I attended the Lindau Nobel Laureate meeting in Germany. This meeting is like no other, because it brings together 30 Nobel laureates and 500 young scientists in an amazing atmosphere. These Nobel laureates were like rock stars to us, and I have rarely felt so much scientific enthusiasm traversing the whole audience of a meeting. I would say this meeting was a game changer for me, and it still fills me with excitement.

Who are your role models in science? Why?

My role models in science are mostly strong women that manage to juggle excellent scientific work and a fulfilling private life. As a kid, my grandmother, a geneticist, used to tell me stories about her youth as a researcher back in the 1950s in Bulgaria, my home country. I was amazed by the world she described to me, so peculiar and different from what I was used to. Back then, science was subject to political indoctrination, and scientific discoveries had to be 'approved' by the authorities in order to be published or presented at a conference. I was strongly inspired by this story and this gave me the motivation to pursue a career in science.

What's next for you?

I recently defended my PhD and I am currently looking for a postdoctoral position. I am interested in dynamic processes in cell biology where cells interact with each other or with their microenvironment, for example in the field of epithelial homeostasis. As a microscopy enthusiast, I am convinced that 'seeing is believing', so I would like to work on processes that are amenable to live imaging.

"Research can sometimes be like a boxing ring…"

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

During the hard times of my PhD, I felt the urge to find a way to release all of the accumulated tension. This is when I became interested in martial arts, discovering with amazement how crucial it is to stay active in tough times. Research can sometimes be like a boxing ring, and practicing sport efficiently taught me to take the hits and keep standing.

Reference

Staneva, R., El Marjou, F., Barbazan, J., Krndija, D., Richon, S., Clark, A. G. and Vignjevic, D. M. (2019). Cancer cells in the tumor core exhibit spatially coordinated migration patterns. *J. Cell Sci.* **132**, jcs220277.