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FIRST PERSON

First person – Bertille Bance and Shailaja Seetharaman

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. Bertille Bance and Shailaja Seetharaman are co-first authors on 'Microtubule acetylation but not detyrosination promotes focal adhesion dynamics and astrocyte migration', published in JCS. Bertille is a post-doc in the lab of Marc Sanson, at The Brain and Spine Institute (ICM), Paris, France, where she is interested in mechanisms controlling cell proliferation, polarity and migration in normal and tumor cells. Shailaja is a PhD student in the lab of Sandrine Etienne-Manneville at Institut Pasteur, Paris, France investigating the role of the cytoskeleton in cell migration and mechanotransduction.

Bertille Bance

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

BB: Directed cell migration is an essential process in the development and maintenance of organisms. In adults, it is involved in wound healing and immune responses. However, migration can also contribute to pathological processes such as tumor formation and metastasis. It is therefore important to understand cell migration at a molecular level in order to find new therapeutic approaches. Specific cellular structures such as the cytoskeleton maintain cell shape and allow cell movement. Microtubules, as part of the cytoskeleton, are involved in the regulation of cell migration. Microtubules can be decorated by small motifs called post-translational modifications (PTMs). In this project, we focused on two of these PTMs, microtubule acetylation and detyrosination, whose biological functions are not well understood. We observed that microtubule acetylation is involved in the dynamics of the cell anchorage to its microenvironment, which is mediated by focal adhesions.

SS: Cells in our body are constantly moving during development, tissue repair, wound healing, etc. Cell migration is also involved in diseases such as cancer and therefore our aim is to understand how this process is regulated.

During migration, cells attach to their surroundings and exert forces in order to move, just as a snail in the garden would do in order to move. These points of attachment of the cell to its surroundings are called focal adhesions.

Our paper is primarily focused on one of the skeletal structures of the cell, called microtubules, in regulating cell migration. This work describes a comparison between two modifications of microtubules that were always thought to perform similar functions. We show that one of the modifications of microtubules, acetylation, regulates cell migration by promoting the formation and disassembly of focal adhesions.

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

BB: Two considerable challenges in this project were the absence of tools to observe microtubule acetylation live and the lack of an anti-αTAT1 antibody that works for immunofluorescence. Because this study was based mainly on cellular dynamics, we couldn't directly observe endogenous αTAT1 or microtubule acetylation in live cells. To overcome this, we carried out several experiments on fixed and live cells, did a lot of biochemistry and microscopy to try and make sure that our results were consistent, and had good controls. Finding the tools to observe αTAT1 and microtubule acetylation in live cells is a substantial challenge in the coming years, but is necessary to fully understand the functions of microtubule acetylation.

SS: As Bertille mentioned, we've had difficulties in studying microtubule acetylation live due to the lack of tools. We are currently working towards better characterizing αTAT1 and maybe, in a few years, we will be able to study the dynamics of acetylated microtubules and αTAT1.

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

BB: My 'eureka' moment was when I finally managed to stain astrocytes with both focal adhesions and microtubule acetylation markers simultaneously, after spending a long time trying different fixation protocols and antibodies.

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

We chose JCS because of the broad audience of cell biologists that it caters to. In addition, JCS publishes a huge number of articles on the cytoskeleton–organelle interface, cell polarity and migration, and

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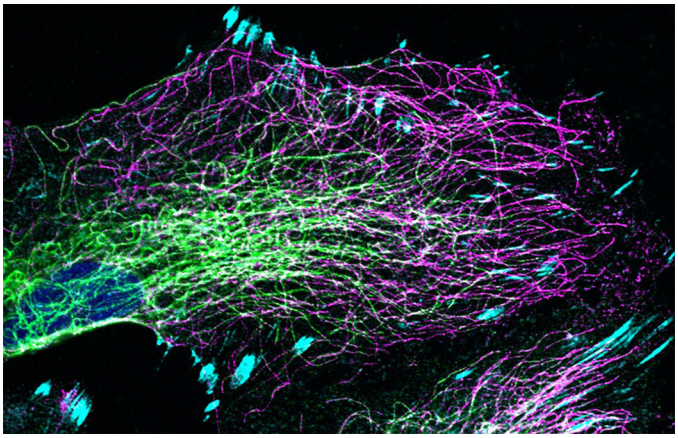
Shailaja Seetharaman

therefore, we felt that our paper would be apt for this journal and would reach more researchers in this field.

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

BB: I worked on this project during my PhD so all the advice from researchers and experts on PTMs was very useful. I also remember the guidance of the researchers in the lab, who were always available for technical issues and moral support. The discussions I had with experts in the field such as Bruno Goud and Carsten Janke, who agreed to be a part of my thesis committee meeting, provided valuable input throughout the course of my PhD.



Migrating astrocyte stained for alpha-tubulin (magenta), acetylated tubulin (green), talin (cyan) and DAPI (blue).

SS: My supervisor, Dr Sandrine Etienne-Manneville, has been an inspirational mentor. During the time that I've been working with her, I've learnt a lot about time management and the balance between work and personal life. Apart from being a wonderful supervisor, what really stands out is that Sandrine is very enthusiastic and open-minded when it comes to science. She has always provided me with the independence and freedom to work in my style and this has immensely helped with my productivity. My (long) chats with Sandrine are always fun and I believe that the rapport between a PhD student and their supervisor has a huge effect on the student's progress, both scientifically as well as personally.

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?

BB: I've always been happy and excited every time an experiment worked well and I could progress in a project. I'm always in a hurry to know if my hypothesis is right and if my experiment worked. We always learn and have technical challenges to accomplish. I love science and I love fundamental science. Without fundamental science, there is no progress in medical therapy. So I would like to continue to do what I love and contribute to the global understanding of the living world.

SS: My family has always been very supportive and have encouraged me to pursue science right from when I was in school. In particular, my sister recognized my interests and skills during high school and motivated me to pursue a career in biology. When I started doing research, I realized that I am very excited to learn new techniques and to carry out experiments. I have always been amazed by the wonders of nature and how a living system functions the way it does. The fact that I'm able to explore and find new things that no one has described before drives me to be more curious and to work harder.

Who are your role models in science? Why?

BB: It's not very original, but Marie Curie's life is impressive, not just in what she brought to science but also in her pugnacity and strength. I also admire Professor Francoise Barré Sinoussi, who was awarded the Nobel Prize for discovering HIV. Not only has she had an amazing career, but she also been very involved in training of young researchers and defending fundamental research.

SS: During my master's, I worked with Professor Anne Ridley at King's College London (who's now at the University of Bristol, UK). Anne has published several groundbreaking papers on Rho GTPases and cell migration. Back in the 90s, she showed that Rho and Rac altered the cytoskeleton to regulate cell migration and this led to the start of a whole new field. She was recently elected as a Fellow of the Royal Society for her immense contribution to cell biology. As well as being a great scientist, Anne is very down to earth and treats everyone equally. She was always keen on listening to my ideas and gave me the freedom to make decisions even as a master's student. I learnt a lot from working with Anne, such as professional ethics, and organizing, prioritizing, designing and planning experiments efficiently – the list goes on! Her support and encouragement through the rough times made me stronger and I am thankful for all the motivation she has given me throughout my career so far.

What's next for you?

BB: I'm now a post-doc in Professor Marc Sanson's lab at the Brain and Spine Institute, where I still do fundamental research but with more proteomics and biochemistry approaches and in direct collaboration with physicians.

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SS: I plan on continuing in academia and will start looking for postdoc positions towards the end of this year. I would like to continue to explore the role of the cytoskeleton in regulating cell migration and mechanotransduction.

Reference

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