

FIRST PERSON

First person – Tiina Viita

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. Tiina Viita is first author on 'Nuclear actin interactome analysis links actin to KAT14 histone acetyl transferase and mRNA splicing', published in JCS. Tiina is a PhD Student in the lab of Maria Vartiainen at the Institute of Biotechnology, University of Helsinki, Finland, investigating the nucleus, proteomics, chromatin remodeling, actin and post-translational modifications of histones.

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

Cells control their behavior through the cell nucleus, which contains the genetic material, DNA. During gene expression, genetic information from DNA is converted into functional protein with the help of the nuclear gene expression machinery. It is important that this machinery works flawlessly (during, for example, embryonic development) and that the right genes are expressed at the right time and in the right place. Changes in this delicate system affect cell behavior and can sometimes drive normal cells to become cancer cells. Actin is an important cytoplasmic protein, which has also been linked to different nuclear processes related to gene expression. Although there are many studies showing that actin is involved in nuclear actions, the role of direct binding partners, and thus molecular mechanisms, has remained unclear. In our study, we were able to identify multiple putative nuclear actin-binding partners (the nuclear actin interactome) by using two different mass spectrometry approaches (AP-MS and BioID). Further investigations with these interaction partners revealed that actin might control gene expression in a new fashion by altering histone modifications via the histone acetyltransferase KAT14. Our results with BioID linked actin to several steps of transcription as well as to RNA processing. Interestingly, alterations of actin levels in the nucleus disturbed alternative splicing, which could suggest that nuclear actin might control transcription elongation rate. Therefore, our findings have emphasized the role of actin in different gene expression steps and our interactome data can be used as a platform for further mechanistic studies.

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

I think the biggest challenge of this project was to figure out how to distinguish actin interactions in the nucleus from the ones in the cytoplasm. Actin is an essential component of cytoskeleton and it can shuttle in and out from the nucleus, so we really needed to think outside the box to obtain the nuclear actin interactome. It was my supervisor's idea to enrich the amounts of actin in the nucleus by adding a nuclear localization signal to tagged actin. By doing so, we were able to compare interactive proteins from the cytoplasmic actin pool against the nuclear actin pool, which then allowed us to obtain specific proteins that interact with nuclear



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actin. Further experiments with a subset of these proteins showed that, indeed by these means, we have been able to reveal novel nuclear actin-binding proteins. I hope that our nuclear actin interactome can help other scientists to determine the molecular mechanisms behind the nuclear functions to which actin has linked before this publication.

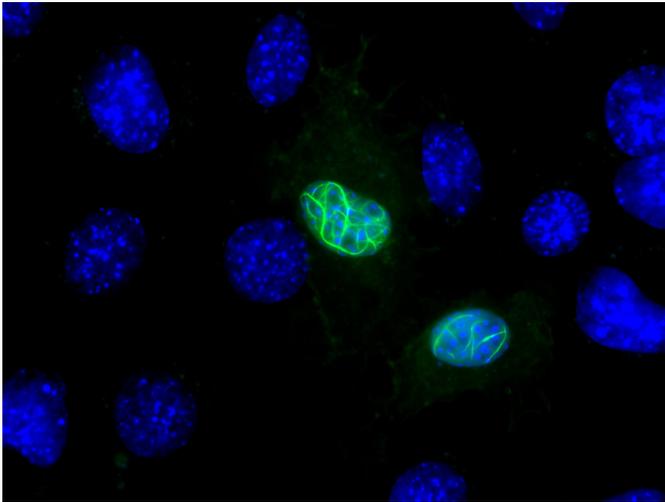
When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

I don't have any particular result in mind, but rather the amazing feeling you get after a successful experiment. Let's face it, in research you have to deal with disappointments in the form of failed experiments or wrong hypotheses. For myself, I think that less than 15% of all of my experiments have given me a direct answer to the problem that I have tried to solve and, more often, the results lead you to new questions and ideas. However, the rare moments when the results match your hypothesis are so motivating and energizing. This particular feeling of great success is the one thing that has kept me within scientific research and still does.

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

We wanted to publish our study in a great journal, which is widely read by cell biologists. I personally have enjoyed reading Journal of Cell Science as the studies presented in this journal are well executed, and often bring new insights into the molecular mechanisms behind certain biological events.

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Bimolecular fluorescent complementation (BiFC) with split GFP attached to nuclear localizing actin (NLS-GFP1-10-Actin) and actin-binding protein (GFP11-Drebrin) drebrin. This caused interesting actin filament structures inside the nucleus, which could be observed through GFP.

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

To this, I have to say my lab mates, as all of us have faced the same obstacles in our work, and we can support one another when things are not going smoothly. I think other scientists can understand your passion for science possibly better than your non-scientist friends, and for this reason support and understanding from your colleagues is a big bonus.

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 most interesting and game-changing moment for me career wise was when I realized why I want to continue in science. The spark for scientific research came from my master's thesis supervisor, Juha Savinainen, from the University of Eastern

Finland, who offered me an interesting master's thesis project. Juha and my other supervisor, Jarmo Laitinen, mentioned that the most interesting projects should be given to students as they are the future researchers. Now I could not agree more, as during my thesis project I realized how rewarding it was to explore something completely new and get interesting data, which even puzzled my supervisors. This encouraged me to continue my career towards PhD studies and to this point.

Who are your role models in science? Why?

As a working mother, I admire successful female scientists who have shown me that it is possible to combine work and family. I especially look up to my supervisor, Maria Vartiainen, who was able to get a highly competitive European Research Council (ERC) starting grant for her nuclear actin research, and has taught me basically everything I know about cell biology.

What's next for you?

I will graduate this month and I am planning to carry out post-doctoral research outside of Finland. I have already thought about the place to go, but some arrangements need to be made before I can start the next step of my career. I would like to continue investigating chromatin remodeling or RNA splicing as I had a small glimpse of these fields when putting together this paper.

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

I have been breeding Siamese cats for nearly eight years and there have been six litters in that time. I just absolutely love the elegant appearance and very social personality of these cats. Cat breeding is an interesting hobby and my knowledge of genetics has been handy when I have been thinking, for example, of how different color patterns might be inherited by the kittens.

Reference

Viita, T., Kyheröinen, S., Prajapati, B., Virtanen, J., Frilander, M. J., Varjosalo, M. and Vartiainen, M. K. (2019). Nuclear actin interactome analysis links actin to KAT14 histone acetyl transferase and mRNA splicing. *J. Cell Sci.* **132**, jcs226852. doi:10.1242/jcs.226852