© 2020. Published by The Company of Biologists Ltd | Journal of Cell Science (2020) 133, jcs254615. doi:10.1242/jcs.254615

FIRST PERSON

First person – Sampo Kukkurainen

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. Sampo Kukkurainen is first author on 'The F1 loop of the talin head domain acts as a gatekeeper in integrin activation and clustering', published in JCS. Sampo conducted the research described in this article while a PhD student in Vesa Hytönen's lab at Tampere University, Faculty of Medicine and Health Technology, Tampere, Finland. He is now a researcher at Tampere University Hospital. His PhD was on the mechanobiology of talin and integrin, analyzing their atomic level interactions using computational structural biology tools.

Sampo Kukkurainen

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

Cells actively move, spread and respond to signals from their environment. Many of these functions require integrins, which are proteins that stick out from the cell surface like tiny fingers. Integrins help cells to feel their surroundings, and to take a firm grip when and where the cell needs to adhere. Inside the cell, a protein called talin works like a switch that controls integrins; talin can bind to the tail of integrin within the cell, making the fingers on the outside of the cell extend and the cell attach. Our study focuses on a specific flexible part of talin, which had been thought to mainly anchor talin to the cell membrane. Our results show that this flexible part of talin forms direct contacts with integrin and appears to be an important part of the mechanism that activates integrins.

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

Our simulation data suggested that the F1 loop of the talin head interacts with integrin, and integrin clustering data indicated that certain residues in the loop are critical for controlling integrin activity. But how could we verify that such an interaction does take place in cells? We finally overcame this challenge by cysteine scanning of the proposed contact regions in integrin and talin. This way, we were able to introduce covalent bonding between proximal residues in integrin and talin, and to reveal the contact interface.

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

At the beginning of this project, we speculated that an active talin head might have a conformation similar to other members of its protein family, although this would not be consistent with published crystallographic data. Our study therefore started off as a high-risk project, in which we carried out simulations of a partially modeled talin head to make predictions of talin conformation and function. There definitely were some 'eureka' moments as bits and pieces of evidence from the lab started to accumulate in support of our hypotheses, such as when the interaction between talin F1 loop and integrin was confirmed in cells, or when mass spectrometry provided evidence for a compact talin head. Overall, I was amazed by the power of simulations of molecular dynamics in predicting protein structure and function in this project.

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

We wished to bring our findings to the vast integrin signaling research community. We found Journal of Cell Science to be the right platform to reach our target audience, and appreciated its excellent reputation as a non-profit publisher.

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

I have had the opportunity to learn from several people along the way, and it does not feel completely fair to only name a couple of mentors. However, Prof. Vesa Hytönen has been an invaluable support as my PhD supervisor, and an inspiring person to work with. I would also like to mention Prof. Bernhard Wehrle-Haller, who never ceases to amaze me with his in-depth knowledge of everything associated with integrin signaling.

What's next for you?

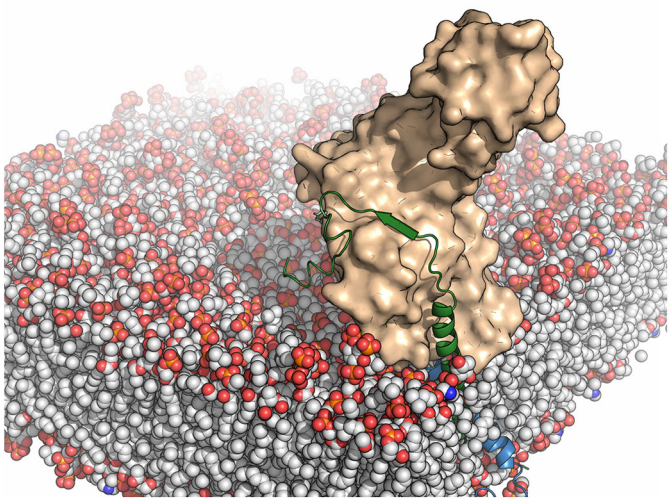
At the moment, I am working as a researcher at Tampere University Hospital, harmonizing and analyzing health data for research. I enjoy the new challenges that come with real world data, and the possibility to contribute to diverse research projects.

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

I like to unwind by riding horses and learning the Mongolian language.

Sampo Kukkurainen's contact details: Tampere University Hospital, P.O. Box 2000, FI-33521 Tampere, Finland.
E-mail: sampo.kukkurainen@outlook.com

Journal of Cell Science (2020) 133, jcs254615. doi:10.1242/jcs.254615



Talin head in complex with membrane-embedded αIIbβ3 integrin. The figure is a snapshot from a 1-µs molecular dynamics simulation. Talin is shown as a light brown surface, αIIb and β3 integrins as cartoon and colored blue and green, respectively.

Reference

Kukkurainen, S., Azizi, L., Zhang, P., Jacquier, M.-C., Baikoghli, M., von Essen, M., Tuukkanen, A., Laitaoja, M., Liu, X., Rahikainen, R. et al. (2020). The F1 loop of the talin head domain acts as a gatekeeper in integrin activation and clustering. *J. Cell Sci.* **133**, jcs239202. doi:10.1242/jcs.239202