

FIRST PERSON

First person – Eike Mahlandt

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. Eike Mahlandt is first author on 'Visualizing endogenous Rho activity with an improved localization-based, genetically encoded biosensor', published in JCS. Eike is a PhD candidate in the lab of Joachim Goedhart at Department Molecular Cytology, Swammerdam Institute for Life Sciences, Amsterdam, The Netherlands, where she develops molecular tools to study protein activity in real-time in vascular endothelial cells using fluorescent microscopy.

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

Cells are motile; they actually move tremendously. In the same way as the human body needs the skeleton and muscles to move, individual cells possess the actin cytoskeleton (see figure), which enables cellular movement and migration. Where the human body needs the brain to control movement, cells use regulatory proteins to control the actin cytoskeleton. We focus on one group of proteins that function as a molecular switch to become activated and thereby regulate the actin cytoskeleton. For example, when switched on, the G-protein Rho initiates cell contraction via actin disassembling. We want to know where in the cell the protein is active. Therefore, we improved a genetically encoded, fluorescent Rho biosensor to mark the areas of the cell where Rho is active in real time. The next step is to image in real-time the activity of multiple GTPases at the same time. Using single-color sensors will help to image multiple biosensors in one cell at the same time.

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

Our biosensor binds endogenous Rho, so the expression level should be low in order to prevent the inhibition of the natural Rho signaling. Therefore, we decided to work with a low-expression promoter. Additionally, the plasmid has a low transfection efficiency. Hence, I spent a significant amount of time gazing into the darkness at the microscope hunting for the one cell that shows low fluorescence.

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

Once we had identified the optimal bio sensor for Rho, we proceeded to make a stable cell line. After looking at the seemingly endless darkness, it was amazing to see the stable cell line for the first time at the microscope, with each and every cell glowing in the dark!

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

We first submitted to Review Commons, where a paper is reviewed before submitting to a specific journal. After we received the reviewer comments we were able to choose to submit our article



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together with the reviewers' comments and the rebuttal to a journal. JCS is participating in the Review Commons process and we found it was a perfect fit for our article.

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

My direct supervisors Jaap van Buul and Joachim Goedhart show great energy together and our work discussions always inspired my work. The collaboration between our two labs made it possible to generate a stable cell line of the Rho sensor expressed in endothelial cells. Plus, the collaboration gave me the opportunity to image the biosensor at the lattice light sheet microscope in the advanced imaging center of Janelia as a side project during our research visit.

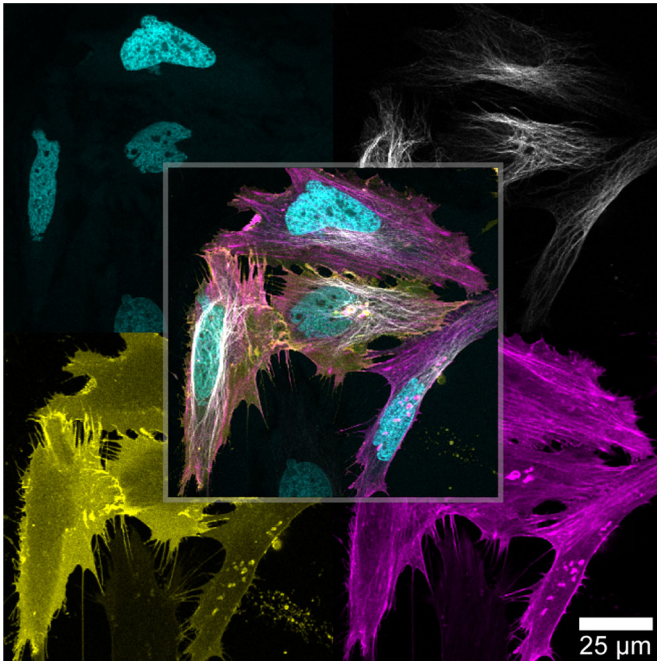
What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

I enjoy the freedom of my PhD project, to implement my own ideas and create new molecular tools. During my Master's studies, I enjoyed the fluorescent microscopy experiments the most, so I knew I wanted to learn more about this technique. Now, towards the end of my PhD project, not much has changed and I still love doing microscopy.

Who are your role models in science? Why?

I admire the female researchers of the last centuries such as Clara Immerwahr and Mileva Marić but also Nancy Hopkins, who smoothed the path for the female researchers of my generation.

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Confocal microscopy image of four different genetically encoded fluorescent markers in living HeLa cells. Shown are actin (magenta) marked with LifeAct-HaloTag (JF635nm), the nucleus (cyan) marked with H2A-mTurquoise2; microtubules (gray) marked with EMTB-mNeonGreen; and the plasma membrane (yellow) marked with Lck-mCherry.

Reading their biographies showed me how much passion they had for their work and their willpower to overcome obstacles.

What's next for you?

I will finish my PhD project by the end of 2021 and I enjoy research so much that I would love to continue my career in research, preferably with a microscopy-related project.

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

My favorite experiment is 'AgarArt', which is drawing on agar plates with bacteria that express a fluorescent protein, then putting the seemingly empty plate in the incubator, to find a glowing piece of art the next morning when the bacteria have grown.

Reference

Mahlandt, E. K., Arts, J. J. G., van der Meer, W. J., van der Linden, F. H., Tol, S., van Buul, J. D., Gadella, T. W. J. and Goedhart, J. (2021). Visualizing endogenous Rho activity with an improved localization-based, genetically encoded biosensor. *J. Cell Sci.* **134**, jcs258823. doi:10.1242/jcs.258823