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FIRST PERSON

First person – Miesje van der Stoel

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. Miesje van der Stoel is first author on 'DLC1 is a direct target of activated YAP/TAZ that drives collective cell migration and sprouting angiogenesis', published in JCS. Miesje is a PhD student in the lab of Dr Stephan Huveneers at Amsterdam University Medical Center, The Netherlands, where her main research interest is studying how the stiffening of blood vessels can affect vascular integrity and the regulation of endothelial junctions.

Miesje van der Stoel

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

The luminal layer of blood vessels is covered by a monolayer of endothelial cells, which maintains vascular integrity. During aging, blood vessels become stiffer and promote vascular malfunctioning. Endothelial cells sense matrix stiffness through integrin-based focal adhesions, which in turn drive YAP/TAZ signaling. YAP/TAZ control various important cellular functions, such as proliferation, migration and the formation of new blood vessels. YAP/TAZ mediate these processes by inducing the transcription of genes. We have discovered that deleted-in-liver-cancer-1 (DLC1) is a direct transcriptional target of YAP/TAZ upon matrix stiffening. We found that endothelial DLC1 is needed for focal adhesion dynamics, endothelial cell migration and the formation of blood vessels. Our findings identify DLC1 as a key novel player in YAP/TAZ signaling in dynamic endothelial tissue, and we suspect DLC1 is implicated in YAP/TAZ-driven flow sensing and the development of stiffness-related vascular diseases.

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

When we discovered that DLC1 protein expression is promoted by substrate stiffness, we hypothesized that DLC1 might be a transcriptional target of the YAP/TAZ–TEAD complex. To substantiate this, I first looked into publicly available genome and ChIPseq data. The moment that we saw a TEAD motif in the DLC1 promoter region, corresponding to a peak of TEAD binding, felt like a true eureka moment. These insights gave me the confidence that our hypothesis was true! Next, it was relatively straightforward to design functional experiments to test and prove that YAP/TAZ indeed drives DLC1 expression in endothelial cells.

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

Many important and beautiful papers in the fields of endothelial biology, YAP/TAZ signaling and integrins are published in JCS. We therefore felt that JCS could be a great platform for our paper.

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

During this project I was well supervised by my PI, Dr Stephan Huveneers. I could always approach him for support, questions or critical discussions about various cell biological processes. Also, he gave me the opportunity to work independently and introduce my own ideas to the research. Working together with him taught me a lot about how to organize my research projects; how to approach, analyze and think critically about the data obtained, and how to put it into the scientific context.

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?

During my Master's program I performed a really challenging research internship in the field of extracellular matrix remodeling. This was my first encounter with real science and soon I noticed that it is an environment with many challenges and opportunities to develop yourself. This internship was one of my best educational experiences, because besides laboratory techniques, it taught me scientific thinking, writing and setting up experiments. After I completed my Master's degree, it was clear to me that I wanted to improve these skills, which motivated me to apply for a PhD position in the Huveneers group.

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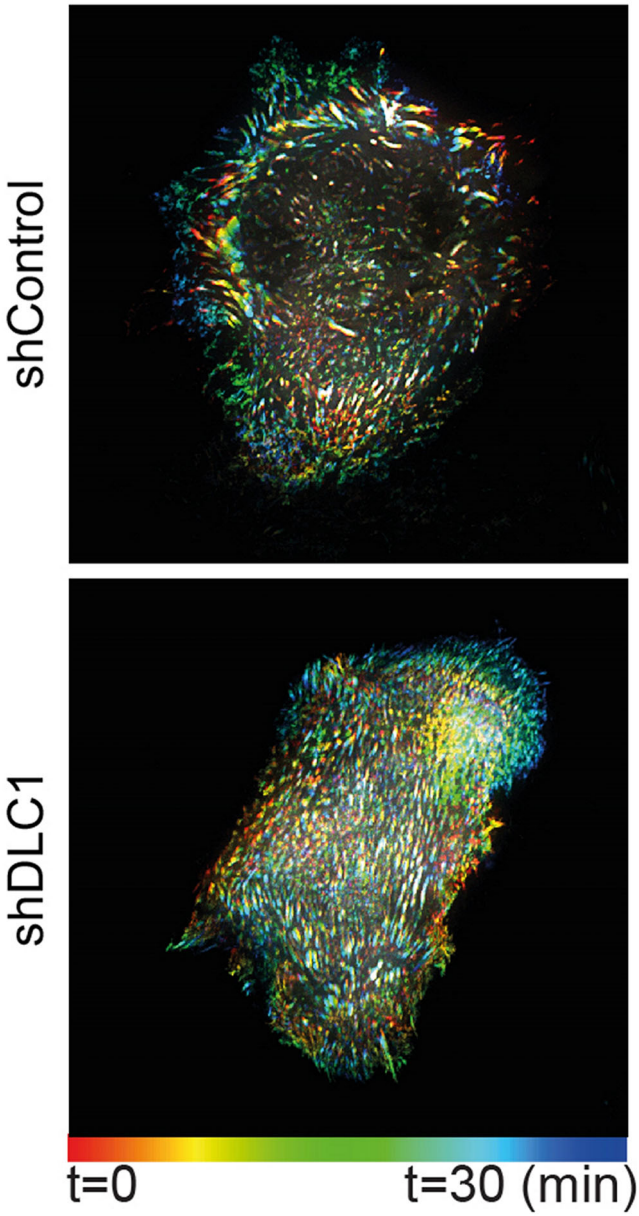

The heat map shows the focal adhesion dynamics in control HUVECs and HUVECs depleted for DLC1 over 30 min in a unique color per time frame. Images are obtained by TIRF-microscopy of HUVECs transduced with shControl or shDLC1 and paxillin–mCherry.

What's next for you?

Next, my objective is to focus on deciphering the role of DLC1 in YAP/TAZ mechanosensing and how DLC1 controls focal adhesion turnover. For me personally, my next goal is to finish my PhD and find a new challenge. If I decide to continue in science, I would like to look for a postdoc position abroad, where I would like to translate my *in vitro* research skills into an *in vivo* model. Otherwise, I want to work in the pharmaceutical industry, where I would like to be involved in bridging the gap between science and business.

Reference

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