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FIRST PERSON

First person – Lilian Sluimer

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Lilian Sluimer is first author on 'SKOR1 mediates FER kinase-dependent invasive growth of breast cancer cells', published in JCS. Lilian conducted the research described in this article while working on this research as a first-year master's student and continued working on this project as a research technician for a year in Patrick Derksen's lab at UMC Utrecht, The Netherlands. She is now a PhD student in the lab of Anna Akhmanova at the Division of Cell Biology, Neurobiology and Biophysics, Utrecht University, The Netherlands, investigating the organization and dynamics of cytoskeletal microtubule networks in different cellular systems.

Lilian Sluimer

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

High-grade and triple-negative breast cancer (TNBC) is an aggressive breast cancer type, and is difficult to treat due to the lack of response to standard chemotherapies and hormone receptor antagonist treatments. A promising candidate for targeted therapy is FER kinase, which is highly expressed in TNBC, correlates with poor survival in TNBC patients and promotes proliferation, invasion and migration of breast cancer cells. Data on how and through which substrates FER kinase controls tumorigenic processes is currently scarce.

In our study, we identified SKOR1 as a novel substrate of FER kinase and an important regulator of breast cancer growth and metastasis. We observed that knockdown of SKOR1 in invasive TNBC cells results in extensive cell spreading and collective growth as non-motile cells. We identified SKOR1-Y234 as the residue phosphorylated by FER, and found that this residue was essential for cellular proliferation and invasion. SKOR1 mediates FER-dependent tumor progression and invasion through regulating actin cytoskeleton dynamics and organization. Together, our findings provide new potential clinical targets for therapies on FER-driven TNBC.

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

Our biggest challenge was that we lacked working phospho-SMAD antibodies to understand whether SKOR1 controls tumorigenic processes through TGFβ signaling. We ran hundreds of western blots with different antibodies but none of them worked in our hands unfortunately. To overcome this, we contacted our collaborator Prof. Peter ten Dijke, a leading expert on TGFβ/SMAD biology, who provided us with TGFβ/SMAD3-inducible luciferase transcriptional reporter constructs. This way, we were able to show that phosphorylation of SKOR1-Y234, a phospho-site identified as candidate target of FER activity, specifically activates SMAD3-dependent TGFβ signaling.

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

The very first time that we performed a knockdown of SKOR1 in the invasive TNBC cell line and we observed massive cell spreading and loss of lamellipodia. We realized that we were at the start of potentially unraveling a completely novel and interesting role for this protein in tumor progression and that felt really cool.

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

Journal of Cell Science has a big audience due to its high-quality articles covering a broad range of subjects in cell biology. Likewise, findings from our study might appeal to researchers from different fields, such as cancer biology and cell migration. We also received valuable comments from the reviewers, which greatly improved our article.

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

Over the past few years, my project supervisor Sandra Tavares grew to be so much more than just a supervisor. From helping me with my very first experiments as a nervous master's student, to giving me the opportunity to independently run and finish my own project after I finished my master's. She was there when I needed advice on both life and lab issues and she made me feel like a very valuable member of our team.

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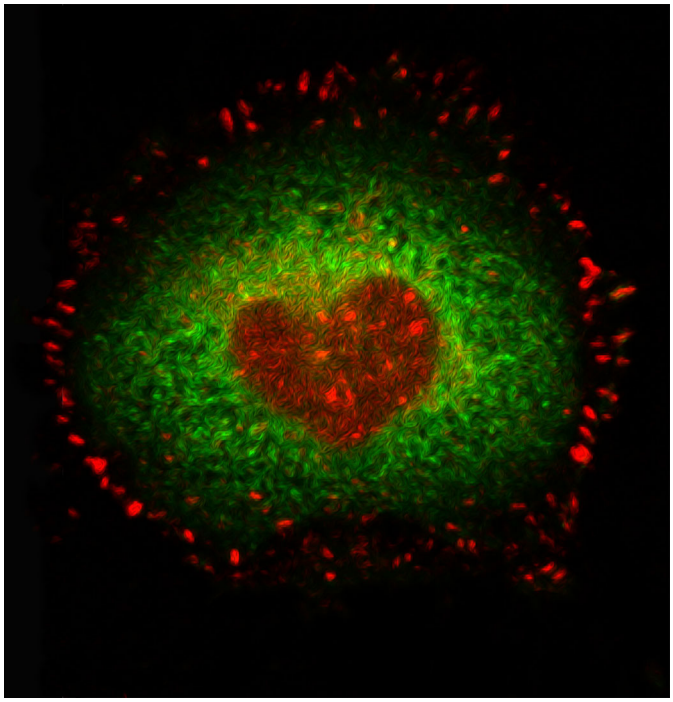

Immunofluorescent staining of an extensively spread breast cancer cell expressing SKOR1-Y234F (green), stained for focal adhesions (red) and DAPI (red). SKOR1-Y234 is the phospho-site targeted by FER kinase and is required for cell migration. Mutating SKOR1-Y234 to Y234F results in cell spreading, loss of lamellipodia and an increase in focal adhesions.

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 really like to work in the lab and to have the freedom to think about my own research questions and ways to answer them. I'm fascinated about cell biology and studying underlying mechanisms of cytoskeletal dynamics and signaling pathways.

Who are your role models in science? Why?

I don't really have a particular role model that I look up to, but I really admire passionate and enthusiastic researchers, who are not just about climbing higher up the academic ladder but really love the science they do.

What's next for you?

I'm currently in my second year of my PhD and I'm really enjoying it! Additionally, I'm passionate about improving sustainability in everyday lab life, so that's also something I'll continue working on.

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

I love road cycling! Ever since the pandemic, I have gone for a ride to relax, clear my head, be outdoors, enjoy the sun and fight the strong Dutch winds.

Reference

Sluimer, L. M., Bullock, E., Rätze, M. A. K., Enserink, L., Overbeeke, C., Hornsveld, M., Brunton, V. G., Derksen, P. W. B. and Tavares, S. (2023). SKOR1 mediates FER kinase-dependent invasive growth of breast cancer cells. *J. Cell Sci.* **136**, jcs260243. doi:10.1242/jcs.260243