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FIRST PERSON

First person – Lizbeth Perez-Castro and Niranjan Venkateswaran

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. Lizbeth Perez-Castro and Niranjan Venkateswaran are co-first authors on 'The AHR target gene scinderin activates the WNT pathway by facilitating the nuclear translocation of β-catenin', published in JCS. Lizbeth is a PhD Student in the lab of Maralice Conacci-Sorrell at UT Southwestern Medical Center, where she is interested in cell molecular biology. Niranjan is a Research scientist in same laboratory where he is interested in understanding the role of essential amino acids in cancer.

Lizbeth Perez-Castro

Niranjan Venkateswaran

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

L.P.-C.: I discovered a new strategy used by cancer to activate molecules that make cells grow and survive environmental stressors. I found that the protein aryl hydrocarbon receptor (AHR) responds to environmental pollutants and small molecules produced by tumors to induce genes (*CYP1A1*, *ALDH1A3*, *ABCG2*, *ADGFR1*, and *SCIN*), which increase the overall fitness of colon cancer cells.

N.V.: Normal cells when exposed to pollutants activate a detoxification program using a protein called AHR. Cancer cells have found a way to hijack this mechanism to its advantage. In this study, we show that the pollutant TCDD and a naturally occurring molecule called kynurenine that is produced in the body, activate a common subset of genes. These genes have been shown to have many critical functions in different types of cancers. Our study highlights how exogenous pollutants can be carcinogens and how endogenous molecules such as kynurenine could also contribute to the development of cancer. Along the way we also identified a unique connection between a protein called scinderin and a well-established cancer pathway called WNT signaling.

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

L.P.-C.: This project was challenging in several ways. First, I began working on it during COVID-19 when I was starting graduate school. Although my colleagues were supportive and helpful, working in isolation was hard. Second, we had numerous unexpected results, which led us to learn more about the field. Third, there were major technical difficulties with some of the experiments including ChIP, which I was sad I was not able to complete. However, I am proud of the careful and rigorous data that is present in our manuscript.

N.V.: Like many projects, we had several technical challenges, but none greater than the challenge of COVID-19. The whole project was done amidst the pandemic. The lockdown and the restrictions severely hampered our ability to do experiments. I am extremely proud of the way my team navigated the lockdown by brainstorming

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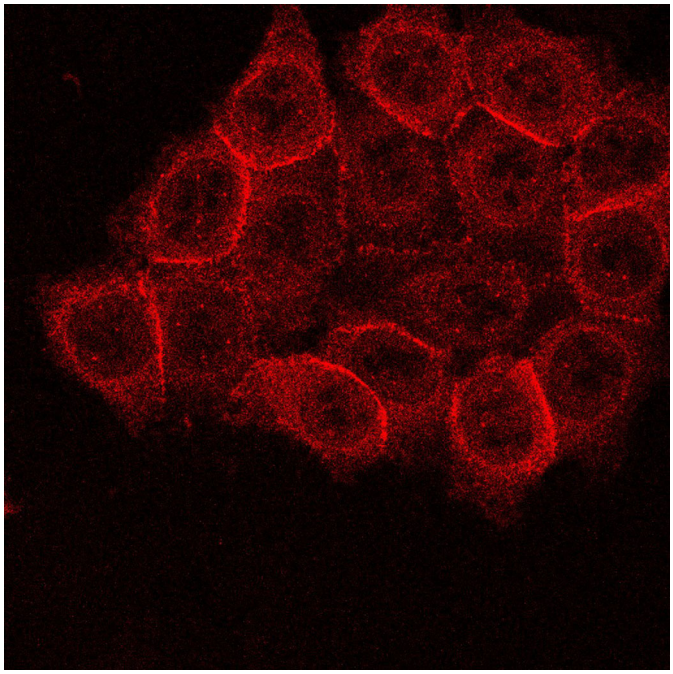

Immunofluorescence image of colon cancer cells that helped us discover that β-catenin is affected by AHR.

ideas and completing key data analysis and compiling several manuscripts and coming out reenergized.

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

L.P.-C.: When we found out that SCIN (an actin-severing protein) was regulated by AHR I decided to perform immunofluorescent staining on the cells. I was expecting to see a change in the actin filaments of these cells, so I decided to use β-catenin just to visualize cell–cell adhesion. To my surprise, I saw that nuclear β-catenin increased upon SCIN expression. This led to a series of experiments that demonstrated that the nuclear levels β-catenin increased with upon SCIN expression, possibly activating the WNT pathway.

N.V.: The big eureka moment for me on this project, was the results of the RNA-seq experiment. This experiment gave us a lot of confidence that we were on the right track. Our experiments validated several of the reported target genes published across various journals. This validation of the known target genes gave us the confidence to go after the novel gene targets we identified from the experiment. Reproducibility is key for success.

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

L.P.-C.: Journal of Cell Science publishes high quality manuscripts in the field of cell biology – I have always read JCS papers and thought it would be a dream to have my first author paper published in JCS. Additionally, the community that reads JCS is my community and is the perfect fit for our story. We hope this study will reach a broad audience and impact the cell science community.

N.V.: This is our first manuscript to be published in the Journal of Cell Science. Over the years, we have come across several quality papers published in this journal, and we believed our paper would strongly appeal to the audience of this journal and the scientific community. We were delighted with the efficient review process and the feedback received. The comments received were fair and improved the quality of the manuscript.

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

L.P.-C.: My PI Maralice Conacci-Sorrell has been a great mentor to me. Beyond helping me grow in the lab, she has helped me develop critical skills and confidence in my abilities to succeed in science. Dr Mari-Carmen Lafita-Navarro, a postdoc in our lab, has helped me along the way. She always asks the tough questions and helps me to work out the answers. My colleagues Niranjan Venkateswaran and Roy Garcia were amazing teammates in the development of this study.

N.V.: Dr Maralice Conacci Sorrell has played a tremendous part in my scientific career. She has been incredibly supportive of all the team members and wants to see everyone succeed. She is a great listener and very generous in sharing her experiences to help navigate difficult situations. Her honest and direct feedback had always made me make better decisions.

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?

L.P.-C.: I've always had a curiosity for science. Growing up I've always wanted to pursue a career in science. As I got older and knew about all the different paths you could follow in science, I realized wanted to understand better the basic of science. Getting a PhD in cell molecular biology will give me the opportunity to contribute knowledge that will hopefully help advance and develop treatments for different diseases.

N.V.: Like many before me, the cliched moment that made me pursue a career in science was the movie Jurassic Park. Molecular cloning, recombinant DNA and genetic engineering became a big fascination and piqued my interest. I still have the same excitement to learn new things and I hope to always be curious about what's next.

Who are your role models in science? Why?

L.P.-C.: My role model in science is Dr Maralice Conacci-Sorrell. She is an inspiring woman in science, she has risen, won several awards and its active in the university. She is one of the most supportive people I've met, she actively advocates for woman and minorities. She has created a collaborative and energetic environment in lab. I can only hope to eventually be as approachable and as great a mentor as she is.

N.V.: Not specific to science, but I have plenty of role models, such as many of my teachers, some of my family and friends, and most importantly my parents who were both amazing teachers. They have all shown me that life is all about those little moments. I aspire to have a healthy work–life balance and enjoy the little moments.

What's next for you?

L.P.-C.: Currently I'm hoping to continue learning even more by doing a postdoc in toxicology.

N.V.: This was one of my last projects in the Sorrell lab, and hence I am very grateful that Lizbeth was able to take over and finish the project. I am currently working as a research scientist at Tavros

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Therapeutics working on identifying the next generation of targeted therapies.

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

L.P.-C.: I was born and raised in Puerto Rico and I skipped kindergarten. Despite my horrible cooking skills, I am a good baker and enjoy making different desserts (especially coffee flavor desserts like macarons and layer cakes).

N.V.: I am an avid follower of European football (Manchester is always Red!! If you know what I mean). Amateur photographer (mostly clicking pictures of my toddler!!).

Reference

Perez-Castro, L., Venkateswaran, N., Garcia, R., Hao, Y.-H., Lafita-Navarro, M. C., Kim, J., Segal, D., Saponzik, E., Chang, B.-J., Fiolka, R. et al. (2022). The AHR target gene scinderin activates the WNT pathway by facilitating the nuclear translocation of β-catenin. *J. Cell Sci.* **135**, jcs260028. doi:10.1242/jcs.260028