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FIRST PERSON

First person – Bhuminder Singh

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. Bhuminder Singh is first author on 'Induction of apically mistrafficked epiregulin disrupts epithelial polarity via aberrant EGFR signaling', published in JCS. Bhuminder conducted the research described in this article while a research fellow in Robert J. Coffey's lab at Vanderbilt University Medical Center, Nashville, TN, USA. He is now an assistant professor at Vanderbilt University Medical Center, investigating the role of EGFR signaling in epithelial homeostasis and disorders such as cancer.

Bhuminder Singh

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

All metazoan body cavities and glands are lined by epithelial cells. Most of these epithelial cells have distinct apical and basolateral surfaces that are segregated by tight junctions. The apical surface faces the lumen of these cavities or tubes, or the outside of the organism, and the basolateral surface is in contact with the underlying tissue. Apical and basolateral surfaces have distinct lipid and protein compositions that are necessary for their proper functions, which include acting as a physical barrier, and selective uptake or release of nutrients and metabolites. As the name suggests, epidermal growth factor receptor (EGFR) signaling is a critical regulator of epithelial homeostasis, which is dysregulated in multiple epithelial disorders including cancer. In this study, we identified that mistrafficking of the EGFR ligand epiregulin to the apical surface leads to aberrant activation of EGFR, which in turn leads to loss of selected aspects of epithelial polarity. Loss of polarity is considered a consequence of epithelial transformation; however, in our study we demonstrate that loss of polarized trafficking of epiregulin (apical mistrafficking) leads to loss of polarity *in vitro* in three-dimensional MDCK Matrigel cultures, as indicated by the formation of ectopic lumens. Thus, our studies show that mistrafficking of a single bioactive ligand can lead to broader loss of epithelial polarity that may have consequences for epithelial transformation.

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

To determine whether ectopic lumens in MDCK cysts form *de novo* after apical mistrafficking of epiregulin, we had to first generate MDCK clones that inducibly express various epiregulin isoforms. We then had to optimize live imaging of the multiple cysts over several days, which was a challenge. We were able to optimize conditions on a Nikon A1R confocal microscope, using laser excitation settings and imaging intervals that allowed the cysts to be viable and proliferative for several days under constant imaging.

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

Microscopy allows us to look at nature in amazing detail. In one such example, when conducting experiments with the basolateral protein epiregulin, we removed the cytoplasmic domain of the protein, and nearly all of the mutant epiregulin then localized to the apical surface, which felt like toggling of a switch to shine light from one side of the cell (basolateral) to the other (apical)!

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

I enjoy reading the high-quality papers published in Journal of Cell Science. This is my second submission to the journal, and I have found the review process professional and fair. During the review of this manuscript, they were understanding of the COVID-related constraints as well.

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

My primary mentor, Dr Robert Coffey, is a constant source of inspiration. His dedication and enthusiasm for science and care for his team members is something I aspire to. Dr Coffey is my strongest advocate and has provided me the freedom, resources and guidance to develop new independent projects. I receive additional inputs from my mentoring committee. I also lean on my peers, who share their valuable personal experiences from the trenches.

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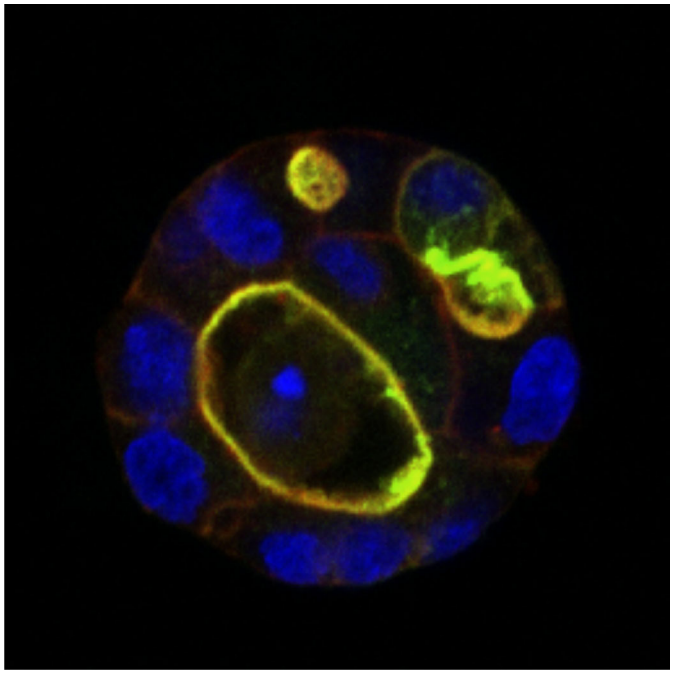

MDCK cysts grown in Matrigel that usually have a single central lumen exhibit ectopic lumens after induction of epiregulin mistrafficking. Green, GFP-tagged mutant epiregulin [(Y156A)EREG–EGFP]; red, phalloidin staining of actin; blue, DAPI staining of nuclei.

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?

It would be hard to find my earliest motivation to pursue a career in science. However, I do remember being fascinated by my high school biology textbooks, where studies of cells interested me the most. I remember borrowing biology books from the public library. Gradually, I have come to appreciate that science is a great way to appreciate the beauty in the world, and it also has the power to make meaningful changes. Finding great role models and colleagues along the way is another plus!

Who are your role models in science? Why?

My colleagues inspire me constantly with their unbound curiosity and work ethic. Of historical figures, Marie Curie holds a special place in my heart due to her perseverance, integrity and contributions to science. Visiting her tomb felt like a pilgrimage.

What's next for you?

I am in the process of setting up my new lab space, and it is very exciting! I look forward to learning the best hiring, training and mentoring practices to build my research team in order to move projects forward.

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

To challenge myself physically, I completed 110 miles of running in June. Although not much of a builder, I was happy to complete fencing my backyard on a slope that was peppered with rocks. Next project: deck extension!

Reference

Singh, B., Bogatcheva, G., Krystofiak, E., McKinley, E. T., Hill, S., Rose, K. L., Higginbotham, J. N. and Coffey, R. J. (2021). Induction of apically mistrafficked epiregulin disrupts epithelial polarity via aberrant EGFR signaling. *J. Cell Sci.* **134**, jcs255927. doi:10.1242/jcs.255927