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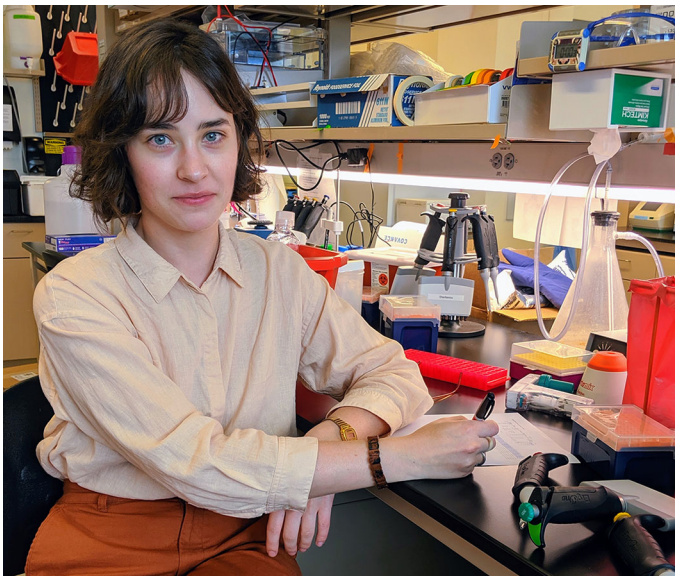
FIRST PERSON

First person – Shelby Bearrows

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. Shelby Bearrows is first author on 'Chromogranin B regulates early-stage insulin granule trafficking from the Golgi in pancreatic islet β-cells', published in JCS. Shelby conducted the research described in this article while a Professional Research Assistant in Dr Samuel Stephens' lab at University of Iowa, Iowa City, USA. She is now a Professional Research Assistant in the lab of Dr Daniel Sherbenou at University of Colorado Anschutz Medical Campus, Aurora, USA, using bioinformatics to understand the mechanisms of drug resistance and dysregulation of protein trafficking in complex diseases.



Shelby Bearrows

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

Insulin is a hormone that regulates blood glucose levels and allows glucose to enter cells, where it is used as an energy source. Proinsulin is converted to insulin and secreted by cells in your pancreas, called islet β-cells. β-cells process proinsulin to insulin inside small vesicles called granules that travel from the Golgi complex to the cell membrane where they release the insulin cargo. If β-cell insulin secretion decreases or if peripheral cells become resistant to insulin, type 2 diabetes can develop. The mechanisms by which secretion of β cell insulin becomes dysfunctional is unknown but vital to understand the development of type 2 diabetes, so we wanted to further understand this pathway. We found that the granule protein chromogranin B plays a vital role in proinsulin processing and insulin secretion. When chromogranin B is absent, glucose-stimulated insulin secretion decreases and proinsulin processing rates decrease. Additionally, the granules are maintained near the Golgi and do not traffic to the membrane as they should. The overall number of granules is also decreased. Taken together, we believe that chromogranin B is vital to correct granule maturation and trafficking as well as proinsulin processing. Further investigations of this pathway might lead to a better understanding of the secretory pathway in β cells and the pathogenesis of type 2 diabetes.

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

Finding a way to track insulin-containing granules at certain time points as they moved from the Golgi to the cellular membrane was extremely challenging. β cells are constantly pumping out insulin, even under basal conditions. However, we needed a way to exclusively look at newly synthesized granules because our previous work lead us to believe that chromogranin B acts at an early stage in the secretory pathway. When we found the SNAP-tag labeling system the project just took off. We were able to generate a SNAP-tagged version of insulin that could be used to exclusively label newly synthesized granules in response to glucose stimulation, in a pulse-chase fashion. Even more exciting was that we engineered it to be used in cell lines as well as in our mouse models, and the images we were able to take in primary tissues are really stunning.

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

Probably when we first started to image insulinoma cells expressing the SNAP-tagged insulin. We used the Interactive Microscope Image Analysis (Imaris) software to convert the image to a 3D plane and to measure the distances from the Golgi as quantitative measures of granule trafficking. It was a very enriching experience to be able to actually see the differences between the chromogranin B knockdown and the control but to also have a numeric output in order to confirm that what we were seeing in all of our other experiments was definitely real.

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

Journal of Cell Science has a reputation for publishing cutting-edge confocal microscopy research and we wanted to select a journal that appreciated this visual aspect of science. Also, glucose homeostasis is extensively studied in other maladies besides diabetes and, so, publishing this in a journal that reaches these investigators was really important to us.

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

Before I joined Samuel Stephens' lab, I had worked in several other labs but had not conducted my own research. I had a small case of imposter syndrome and was worried about my shortcomings, but Dr Stephens believed in me and gave me opportunities I will forever be grateful for. He is also someone who is naturally excited about research and his enthusiasm made the long days at the bench much easier to handle.

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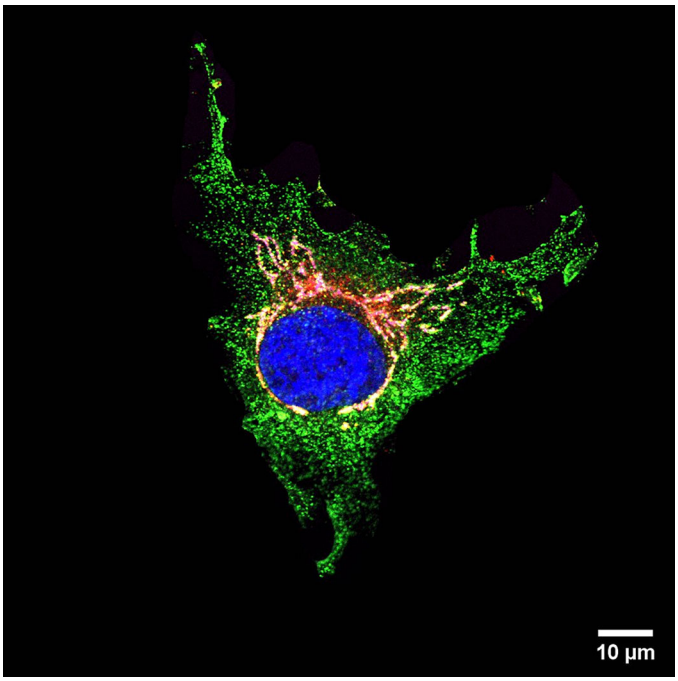

An insulinoma cell stained for insulin (green), hromogranin B (red) and TGN38 (magenta), the nucleus is stained blue (DAPI).

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?

Before I started pursuing a career in biology I was working towards a bachelor's degree in English Literature with a minor in Music Theory. Before that, I was pursuing a bachelor's degree in Electrical Engineering. So, I've definitely given myself the time and experiences to discover what career would suit me best. From these experiences I learned that I want to help people but I also want to be interested in and engaged with my work, so biology was an easy choice. It's definitely a career that will never be boring.

Who are your role models in science? Why?

Probably Bill Nye because of how accessible he has made scientific theory to children and how he continues to advocate science through his numerous outreach programs. He also comes from a very unconventional background. Before he started "Bill Nye The Science Guy", he was working as a mechanical engineer for Boeing, but at night he would go to open mics and perform stand-up comedy because he loved to make people laugh. I don't think I could ever do stand-up, but it's encouraging to hear of other scientists who took round-about ways to achieve their goals.

What's next for you?

I've recently taught myself several programming languages including C, python and R and I am also currently writing an R script to generate a high-throughput data analysis pipeline for my current research at the University of Colorado. This work has taught me how much I enjoy data analysis and so, to further my knowledge of this field, I'll be applying to Bioinformatics Masters programs in 2020.

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

I've recently taken up running. I never thought I'd be a runner but I'm proving to myself that growing up doesn't mean slowing down. Who knows what other hobbies I'll pursue in my life!

Reference

Bearrows, S. C., Bauchle, C. J., Becker, M., Haldeman, J. M., Swaminathan, S. and Stephens, S. B. (2019). Chromogranin B regulates early-stage insulin granule trafficking from the Golgi in pancreatic islet β-cells. *J. Cell Sci.* **132**, jcs231373. doi:10.1242/jcs.231373