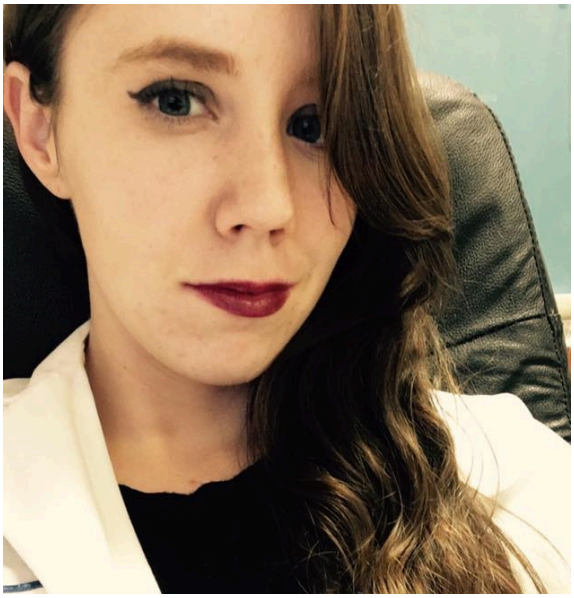
FIRST PERSON

First person – Rishel Vohnoutka

First Person is a series of interviews with the first authors of a selection of papers published in Biology Open, helping early-career researchers promote themselves alongside their papers. Rishel Vohnoutka is first author on 'Influence of a GSK3β phosphorylation site within the proximal C-terminus of Neurofilament-H on neurofilament dynamics', published in BiO. Rishel is a postdoctoral research associate in the Department of Cell and Developmental Biology at SUNY Upstate Medical University, USA, investigating the cytoskeleton and its relationship to cell function (especially axonal outgrowth and maintenance) and disease (cancer, neurodegeneration).



Rishel Vohnoutka.

What is your scientific background and the general focus of your lab?

My undergraduate degree is in clinical laboratory sciences and my PhD is in biomedical engineering and biotechnology. I believe my strong background in physiology and chemistry strongly enhances my ability to approach disease-related research from both a human physiology approach and a cellular/biochemical approach. As a PhD student I studied neurodevelopment and neurodegeneration using cellular models and biochemical approaches. In particular, I focused on the neuronal intermediate filament (IF) cytoskeleton and its role in axonal outgrowth and maintenance. In my current position as a post doctoral associate I will apply my knowledge of the IF cytoskeleton to investigate interactions with focal adhesion complexes and implications for cancer cell invasiveness and proliferative capacity.

"While the building of maps and connections that link together multiple findings into pathways is the job of a scientist, it is still the most intricate and beautiful part of research."

How would you explain the main findings of your paper to non-scientific family and friends?

Our thoughts and consciousness is built and defined by how our brain cells communicate with one another. This communication allows our brain to tell our legs to move for walking, our stomach to tell our brain we're hungry, our brain to think through a math problem, and much more. Our brain cells speak to each other through electrical signals they send down long projections that connect one cell to another cell. You can think of these connections as telephone wires carrying the conversation of the first brain cell to its target. This could be a muscle, in which case the signal could say something like "contract to pick up your fork". In order to build a functioning brain in utero, a huge quantity of 'telephone lines' for communication are set up and these are later streamlined to a smaller number of connections as our brain develops and learns which lines are useful and which are not. As we age, these lines of communication are worn down and the repair mechanisms that used to be active during development and our youth are no longer active. Due to constant wear from daily use and accelerated wear from diseases like dementia and Alzheimer's disease, communication in aged adults can slow. This often shows itself in the form of memory loss which can result from severe damage to the lines of communication between our brain cells and the absence of repair. Therefore, the study of how our brain builds these connections during development and how these procedures are altered in disease can help us to discover ways to treat cognitive decline.

My research focuses on figuring out what types of repair mechanisms (kinases, phosphatases, proteases) function in the cell to build the structural support for these communication lines between cells and what these repair mechanisms do. Using this approach I found that several types of repair mechanisms work together to build the structural support (axonal cytoskeleton) of these communication lines with a very important key player beginning the process (GSK phosphorylation). This particularly important repair mechanism is dysfunctional in Alzheimer's disease and other forms of cognitive decline. Understanding this process helps us to learn how to retrain or deactivate the appropriate repairmen to fix damaged connections observed in neurodegeneration

What are the potential implications of these results for your field of research?

The results provide a clearer explanation for how neurofilaments transport and change conformation to support function of these structural proteins in various stages of axonogenesis. Also elaborated on is a possible explanation for how neurofilaments within the nodes

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of Ranvier that exhibit reduced levels of C-terminal tail domain phosphorylation are capable of persisting rather than being degraded by the kinases that normally target hypo-phosphorylated neurofilaments. Neurofilaments provide the highly stable 'back bone' to axons of neurons and their assembly and maintenance is vital to synaptogenesis and synapse maintenance.

What has surprised you the most while conducting your research?

The wealth of connections between the research of the various intermediate filament scientists, neurodevelopment, various forms of brain cancer, other cytoskeletal elements (actin, microtubules etc.), focal adhesion complexes, and development. While the building of maps and connections that link together multiple findings into pathways is the job of a scientist, it is still the most intricate and beautiful part of research. Playing a role in discovering these connections has been incredible.

What, in your opinion, are some of the greatest achievements in your field and how has this influenced your research?

The discovery of the kinases, motor proteins, phosphatases and protease systems that regulate neurofilament and axonal cytoskeletal dynamics. Using the base of knowledge currently available on these topics, I sought to fill in gaps of what we don't yet understand. For example, how do hypo-phosphorylated neurofilaments transport to build the axonal cytoskeleton without either being degraded or assembling too early (somal aggregates)?

What changes do you think could improve the professional lives of early-career scientists?

Unfortunately, a career in science can be very difficult at any stage due to funding changes, increased entry-level position requirements and an increased pool of applicants available for hire. Having more resources to help young scientists learn how to write grants, run a lab, find a job, etc. could all be helpful. Also, a database that helps locate clear descriptions of the research in labs all over the world, organized by field of research, would help new scientists in their pursuit of postdoctoral positions and good environments in which to seek a permanent position.

What's next for you?

I am just beginning my first postdoctoral research associate position. I hope to complete as many important scientific discoveries in the form of publications as I can in the next 3-4 years in this position. Following this, I am leaning towards an industry career as a scientist due to increased access to tools and resources to perform research. After about 10-15 years from now, I would really like to move up into leadership and/or mentoring roles in a company with the end goal of leading a team that helps to generate cures or treatments for neurodegenerative conditions. There is a lot left to understand about how our neurons connect to one another and how this goes wrong in disease and I want to contribute as much to that as possible.

Reference

Vohnoutka, R. B., Boumil, E. F., Liu, Y., Uchida A., Pant, H. C. and Shea, T. B. (2017). Influence of a GSK3β phosphorylation site within the proximal C-terminus of Neurofilament-H on neurofilament dynamics. *Biol. Open* **6**, doi:10.1242/bio.028522.