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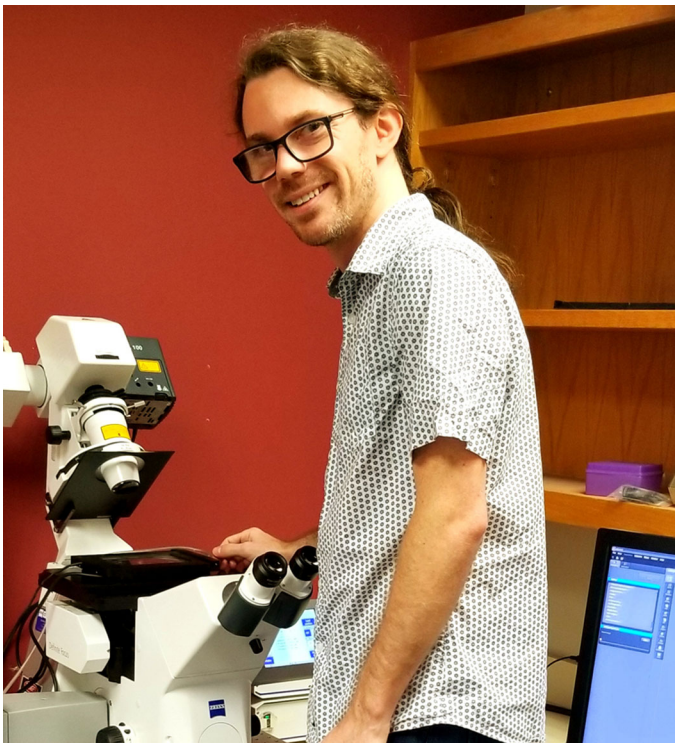
FIRST PERSON

First person – Brian Spurlock

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. Brian Spurlock is first author on 'New quantitative approach reveals heterogeneity in mitochondrial structure–function relations in tumor-initiating cells', published in JCS. Brian is a PhD student in the lab of Kasturi Mitra at University of Alabama at Birmingham, Birmingham, AL, USA, investigating mitochondrial structure and function regulating the self-renewal of normal and neoplastic stem cells.



Brian Spurlock

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

I studied a population of ovarian cancer 'tumor-initiating cells', which initiate tumor formation. Tumor-initiating cells cannot be killed by standard chemotherapy and so are thought to be responsible for relapse. I particularly focused on mitochondria, the cellular structures responsible for producing energy that cells use to divide and carry out their function. Mitochondria in cancer cells are believed to behave differently from those in normal cells, and even between cells from different tumors. Here, I report how the mitochondria of ovarian tumor-initiating cells behave differently from mitochondria in the rest of the cancer cells from the same source. To investigate this difference, I developed a method to study how the structure of mitochondria interacts with their function. I tested the method across several cell types to make sure I could get consistent, verifiable results. By applying this new method to ovarian cancer cells, I identified three cellular states defined by distinct mitochondrial structure and function relationships and demonstrated that tumor-initiating cells need to cycle through these cellular states. The rest of the ovarian cancer cell population could maintain one type of relationship indefinitely. Perhaps if we could prevent this cycling, we could better prevent relapse in all or certain ovarian cancer patients.

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

My mentor and I had trouble convincing ourselves that my validation experiments went far enough to prove that mito-SinCe[2] was broadly applicable and trustworthy. I ended up spending an extra six months primarily working on further validation experiments, including across platforms through bioenergetics profiling. It dramatically improved our story and had the added bonus of demonstrating more potential uses for the method.

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

It was extremely gratifying to find differences in both dynamics and energetics metrics between the population of cells with high mitochondrial membrane potential and the population with low potential. I had seen that the low-potential cells were converted to being high-potential by inhibiting ATP synthesis. This inhibition also selectively killed tumor-initiating cells in culture. I did not yet know, however, what the differences were in how mitochondria were consuming that potential. It was exciting to find not just two but three distinct energetics and/or dynamics states that mapped to membrane potential, with one state appearing to be an intermediate between high- and low-potential states. Finding the intermediate state was important to our hypothesis that tumor-initiating cells cycle between the high- and low-potential states.

Where do you plan to take this project going forward?

I have some preliminary data suggesting that the cycling between energetics/dynamics states is associated with the particular cell cycle of ovTICs. I want to investigate whether regulation of the G1→S transition by mitochondria interacting with cyclin E can maintain tumor-initiating cells by modulating their energetics.

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

I felt our work was in keeping with the mission of the journal. I respect the research reported through JCS and am thrilled to be a part of that legacy. Additionally, my mentor's paper, where this project has its origins, was also published in JCS, so it just seemed fitting.

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

I would be remiss if I did not mention my ninth grade biology I teacher, Mrs Lynda Collins. It was because of her class that I developed an interest in the biological sciences, and her door was always open if I wanted to discuss something I had read or ask for advice. Then Dr Gail Stratton, one of my academic advisors during

Brian Spurlock's contact details: Department of Genetics, University of Alabama at Birmingham, Birmingham, AL 35294, USA.
E-mail: bspurgbs@uab.edu

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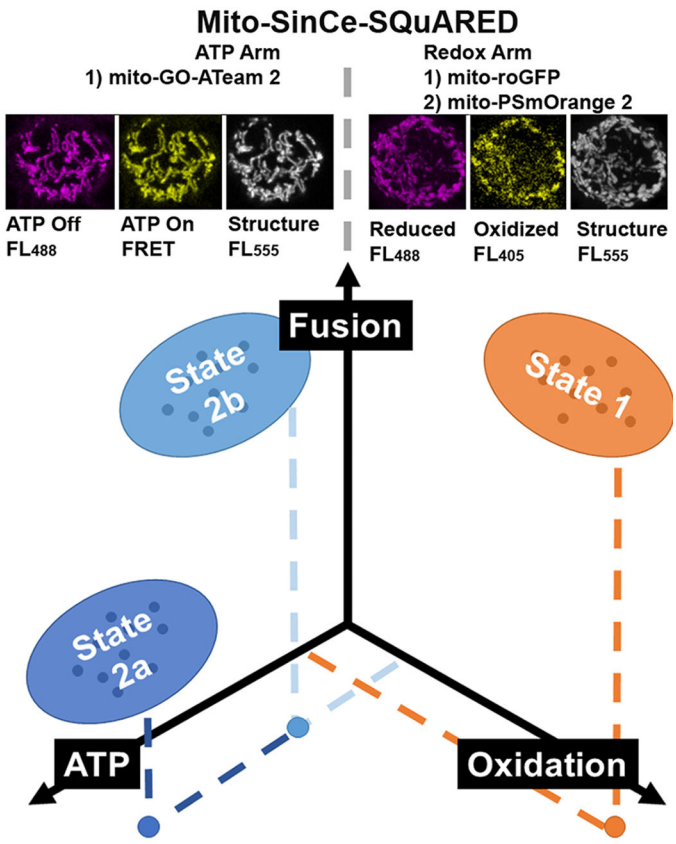

A graphic representation of the application of the two arms of the mito-SinCe2 method to identify distinct energetics/dynamics states in ovarian cancer cells. Representative confocal micrographs show ratiometric energetics probes with compatible structure probes for each arm.

my undergraduate education, helped me design a curriculum that let me meet my degree requirements and pursue my interests to set the stage for me becoming a well-rounded academic. She also helped me by being proudly and visibly queer. Seeing that so early in my training, helped me believe I would not have to sacrifice openness for professional regard. I also want to include my undergraduate biochemistry professor, Dr Susan Pedigo. While I was taking her honors recitation, she told us about auditing a history course across campus because she realized she knew nothing about the topic. I want to follow her example and never stop pursuing topics that interest me. Finally, I have recently been shadowing Dr Samantha Giordano-Mooga in order to learn how to teach undergraduates. Seeing her deal with crisis after crisis, and her trusting me to help, has grown my confidence as an instructor and prepared me to take on courses when I reach that point in my career.

“I latched onto stem cells as a passion that kept me pursuing this career even when I felt discouraged.”

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 mentioned Mrs Collins as a mentor, but it cannot be overstated how much that biology course altered the direction of my life. Thirteen-year-old Brian wanted to be a lawyer, but fifteen-year-old Brian had every intention of studying biology. My budding interest in empiricism started to put me at odds with my religious upbringing, which was occasionally hostile to the ideas of evolution by natural selection and descent from a common ancestor. That is when I discovered Francis Collins’ *The Language of God*, which was valuable to processing the perceived conflict but was more valuable in that one of the appendices discussed regenerative medicine. I latched onto stem cells as a passion that kept me pursuing this career even when I felt discouraged. When I came to UAB, I rotated with Dr Kasturi Mitra to work on two related projects in human pluripotent cells and cancer stem cells. I never left, and that work formed part of the groundwork for this paper.

Who are your role models in science? Why?

I have already mentioned Dr Pedigo, who in addition to being a lifelong learner, also put considerable effort toward advocating for herself and other female faculty in our department. I hope I will always be willing to stick my neck out for myself and other people the way I watched her do. That refusal to be marginalized is a quality I also admire in Dr Mitra, which in addition to the research is part of why I joined her lab. Finally, I admire Dr Joseph Osmundson. In addition to his research as an assistant professor of biology at NYU, he is an accomplished queer essayist and memoirist. It reads as trite even as I type this, but seeing his social media presence and reading his papers on PubMed make me more hopeful about my own career and prospects.

What’s next for you?

I plan to obtain a postdoctoral fellowship, followed by an academic post where I can split my time between researching cellular reprogramming and teaching. I want to do for a new generation what my mentors have done for me.

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

I did improvisational comedy for six years. My first troupe became the first comedy troupe registered with the Mississippi Arts Commission. With my second troupe, I made money doing team-building exercises, professional development conferences, and comedy shows. It led to me playing an intrepid journalist in an episode of the Canadian hicksploitation reality show Mississippi Snake Grabbers.

Reference

Spurlock, B., Gupta, P., Basu, M. K., Mukherjee, A., Hjelmeland, A. B., Darley-Usmar, V., Parker, D., Foxall, M. E. and Mitra, K. (2019). New quantitative approach reveals heterogeneity in mitochondrial structure–function relations in tumor-initiating cells. *J. Cell Sci.* **132**, jcs230755. doi:10.1242/jcs.230755