



mSphere of Influence: Positive Research Culture Enables Excellence and Innovation

 Elizabeth R. Ballou^a

^aInstitute of Microbiology and Infection, School of Biosciences, University of Birmingham, Birmingham, United Kingdom

ABSTRACT Elizabeth Ballou works in the field of medical mycology. In this mSphere of Influence article, she reflects on how two papers by Okagaki et al. (PLoS Pathog 6:e1000953, 2010, <https://doi.org/10.1371/journal.ppat.1000953>) and Zaragoza et al. (PLoS Pathog 6:e1000945, 2010, <https://doi.org/10.1371/journal.ppat.1000945>) made an impact on her career by demonstrating an alternative to destructive publication practices.

KEYWORDS mSphere of Influence, medical mycology, microbiology

Too often, those credited with scientific breakthroughs also enable poor research culture. Examples of gatekeepers, bad actors, and bullies are easy to find throughout the scientific literature, with stories passed on to the next generation through whispered conversations over coffee or in the pub. But how we go about our work, how we interact with our colleagues, and how we train our students have lasting impacts on the course of research. A positive research culture creates space and opportunity for new perspectives, risk, and creativity. These are the drivers of discovery and innovation. Jeremy Farrar, Director of the Wellcome Trust, recently called on each of us to make positive research culture a shared goal (1). The focus of Wellcome reform efforts is on harassment and bullying, and achieving diversity and inclusion goals: systemic challenges that are the domain of universities, funders, and hiring managers. However, we as researchers, collaborators, reviewers, and editors likewise have a role to play in ensuring that the most creative researchers are represented and add their influence to our shared human endeavor.

In my short career, I have twice benefited from the leadership of mycologists in this sphere. In 2009, at the Marine Biology Laboratory's course on Medical Mycology, I met a fellow graduate student, Laura Okagaki, who had an exciting story to tell about an unusual observation that had been long overlooked as an artifact in the literature (2–4). Okagaki was working in the lab of Kirsten Nielsen, then a new principal investigator (PI) at the University of Minnesota, and the two were about to demonstrate the existence of *Cryptococcus neoformans* titan cells as an *in vivo* phenomenon (5). Okagaki was anxious about discussing the story before it was published, but we developed a friendship over our shared interest in *C. neoformans* morphogenesis, and I promised to send her mutants I had generated that we suspected might influence the process (6). Shortly afterward, it became clear that a similar story was being developed in Arturo Casadevall's group, led by postdoc Oscar Zaragoza (7). In some fields, this turn of events has signaled the inevitable end of a career, as high-risk projects that have consumed resources and precious postdoc and graduate student time turn into “me too” papers replicating scooped work.


It took true leadership and a long view of the power of positive research culture to challenge this narrative. Rather than competing to be first to publish, Nielsen and Casadevall worked together and published the reports back to back in *PLoS Pathogens* in 2010 (5, 7). The positive impact of this on the scientists directly involved is obvious:

Citation Ballou ER. 2020. mSphere of Influence: positive research culture enables excellence and innovation. mSphere 5:e00948-19. <https://doi.org/10.1128/mSphere.00948-19>.

Copyright © 2020 Ballou. This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/).

Address correspondence to e.r.ballou@bham.ac.uk.

The views expressed in this article do not necessarily reflect the views of the journal or of ASM.

 Publication doesn't have to be a zero sum game. Leadership from @ACasadevall1 and others shows us a different path towards excellence. @BallouLab

Published 15 January 2020

both labs were able to publish their work in a well-respected journal and received fair and independent reviews unbiased by the artificial shadow of “novelty.” The two papers are distinct in their approaches, and their findings reinforce rather than directly replicate each other, enabling increased confidence in the importance of the phenotype to *C. neoformans* pathogenesis from the wider community. This approach also ensured that both Nielsen and Zaragoza could go on to publish important subsequent work which has been the foundation of a whole field of research with implications for patient outcomes (8, 9).

What may surprise readers is that the wider implications of this leadership are still being felt today. In 2017, I launched my lab at the University of Birmingham, United Kingdom, with the goal of studying mechanisms driving titanization. Despite much effort on the part of Nielsen and Zaragoza’s groups, neither had been able to replicate the phenotype *in vitro*, making mechanistic studies challenging. However, an undergraduate in my lab, Tom Drake, had observed that titan cells can be induced *in vitro* using a simple culture technique, which we subsequently demonstrated is the result of cross-kingdom signaling between fungi and bacteria (10). The discovery was thrilling and opened up rapid access to research avenues that had previously been inaccessible. But my lab at the time consisted of two 6-week summer students and Drake, who was having such fun he just kept turning up every day after graduation. So I reached out to Nielsen to ask if she would be willing to collaborate. She told me two other labs, led by Zaragoza and another new PI, Alexandre Alanio, had already contacted her with similar stories. She was collaborating with Alanio, and they expected to submit the paper within the year.

It was my first time leading a research project and a huge risk to focus my small lab’s efforts and limited funding on an extremely competitive area, particularly now that they knew I was working on a paper. Fortunately, Nielsen immediately encouraged me to contact the editors at *PLoS Pathogens* to ask them to again consider the works as complementary reports. After reaching out to Alanio and Zaragoza and the editor and staff at *PLoS Pathogens*, we were able to coordinate our papers, and all three were published back to back to back in 2018 (10–12). Again, our papers are complementary rather than directly replicative, and our overlapping findings further reinforce the deep signaling events regulating this important morphogenetic switch. The example first established by Nielsen and Casadevall benefited not only the PIs on the three papers, but also our teams, particularly graduate students Hommel and Trevijano-Contador, who led the work in the Alanio and Zaragoza labs. We all continue to work in this space, contributing to a broader understanding of the many interacting signals that drive titanization (13). It has also served as an example for others facing similar competitive choices in our field (14–17).

The practice of scooping and the artificial value we place on being first to publish reveal the lie that science is a meritocracy, where the best research rises to the top. Rather, it is the best resourced that can compete and dictate what work is recognized as excellent and influential. Worse, these practices punish risk taking and innovation in a time when new approaches are most needed to solve the biggest challenges facing society. I am grateful for the leadership shown by Nielsen and Casadevall and for the opportunity to continue to build on this new tradition of science in pursuit of excellence through a positive research culture.

ACKNOWLEDGMENTS

E.R.B. is supported by a Sir Henry Dale Fellowship jointly funded by the Wellcome Trust and the Royal Society (211241/Z/18/Z).

REFERENCES

1. Farrar J. 10 September 2019. Why we need to reimagine how we do research. <https://wellcome.ac.uk/news/why-we-need-reimagine-how-we-do-research>. Accessed 11 December 2019.
2. Feldmesser M, Kress Y, Casadevall A. 2001. Dynamic changes in the morphology of *Cryptococcus neoformans* during murine pulmonary infection. *Microbiology* 147:2355–2365. <https://doi.org/10.1099/00221287-147-8-2355>.
3. Love GL, Boyd GD, Greer DL. 1985. Large *Cryptococcus neoformans* isolated from brain abscess. *J Clin Microbiol* 22:1068–1070.

4. Cruickshank JG, Cavill R, Jelbert M. 1973. *Cryptococcus neoformans* of unusual morphology. *Appl Microbiol* 25:309–312.
5. Okagaki LH, Strain AK, Nielsen JN, Charlier C, Baltés NJ, Chrétien F, Heitman J, Dromer F, Nielsen K. 2010. Cryptococcal cell morphology affects host cell interactions and pathogenicity. *PLoS Pathog* 6:e1000953. <https://doi.org/10.1371/journal.ppat.1000953>.
6. Okagaki LH, Wang Y, Ballou ER, O'Meara TR, Bahn Y-S, Alspaugh JA, Xue C, Nielsen K. 2011. Cryptococcal titan cell formation is regulated by G-protein signaling in response to multiple stimuli. *Eukaryot Cell* 10:1306–1316. <https://doi.org/10.1128/EC.05179-11>.
7. Zaragoza O, García-Rodas R, Nosanchuk JD, Cuenca-Estrella M, Rodríguez-Tudela JL, Casadevall A. 2010. Fungal cell gigantism during mammalian infection. *PLoS Pathog* 6:e1000945. <https://doi.org/10.1371/journal.ppat.1000945>.
8. Zaragoza O, Nielsen K. 2013. Titan cells in *Cryptococcus neoformans*: cells with a giant impact. *Curr Opin Microbiol* 16:409–413. <https://doi.org/10.1016/j.mib.2013.03.006>.
9. Zafar H, Altamirano S, Ballou ER, Nielsen K. 2019. A titanic drug resistance threat in *Cryptococcus neoformans*. *Curr Opin Microbiol* 52:158–164. <https://doi.org/10.1016/j.mib.2019.11.001>.
10. Dambuza IM, Drake T, Chapuis A, Zhou X, Correia J, Taylor-Smith L, LeGrave N, Rasmussen T, Fisher MC, Bicanic T, Harrison TS, Jaspars M, May RC, Brown GD, Yuecel R, MacCallum DM, Ballou ER. 2018. The *Cryptococcus neoformans* titan cell is an inducible and regulated morphotype underlying pathogenesis. *PLoS Pathog* 14:e1006978. <https://doi.org/10.1371/journal.ppat.1006978>.
11. Hommel B, Mukaremera L, Cordero RJB, Coelho C, Desjardins CA, Sturny-Leclere A, Janbon G, Perfect JR, Fraser JA, Casadevall A, Cuomo CA, Dromer F, Nielsen K, Alanio A. 2018. Identification of environmental and genetic factors important for *Cryptococcus neoformans* titan cell formation using new in vitro inducing conditions. *PLoS Pathog* 14:e1006982. <https://doi.org/10.1371/journal.ppat.1006982>.
12. Trevijano-Contador N, de Oliveira HC, Garcia-Rodas R, Rossi SA, Llorente I, Zaballos Á, Janbon G, Ariño J, Zaragoza Ó. 2018. *Cryptococcus neoformans* can form titan-like cells in vitro in response to multiple signals that require the activation of several transduction pathways. *PLoS Pathog* 14:e1007007. <https://doi.org/10.1371/journal.ppat.1007007>.
13. Zhou X, Ballou ER. 2018. The *Cryptococcus neoformans* titan cell: from in vivo phenomenon to in vitro model. *Curr Clin Microbiol Rep* 5:252–260. <https://doi.org/10.1007/s40588-018-0107-9>.
14. Wensing L, Sharma J, Uthayakumar D, Proteau Y, Chavez A, Shapiro RS. 2019. A CRISPR interference platform for efficient genetic repression in *Candida albicans*. *mSphere* 4:e00002-19. <https://doi.org/10.1128/mSphere.00002-19>.
15. Roman E, Coman I, Prieto D, Alonso-Monge R, Pla J. 2019. Implementation of a CRISPR-based system for gene regulation in *Candida albicans*. *mSphere* 4:e00001-19. <https://doi.org/10.1128/mSphere.00001-19>.
16. Pradhan A, Avelar GM, Bain JM, Childers DS, Larcombe DE, Netea MG, Shekhova E, Munro CA, Brown GD, Erwig LP, Gow NAR, Brown AJP. 2018. Hypoxia promotes immune evasion by triggering beta-glucan masking on the *Candida albicans* cell surface via mitochondrial and cAMP-protein kinase A signaling. *mBio* 9:e01318-18. <https://doi.org/10.1128/mBio.01318-18>.
17. Lopes JP, Stylianou M, Backman E, Holmberg S, Jass J, Claesson R, Urban CF. 2018. Evasion of immune surveillance in low-oxygen environments enhances *Candida albicans* virulence. *mBio* 9:e02120-18. <https://doi.org/10.1128/mBio.02120-18>.