Finding your unique path in science

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ABSTRACT **I always found it curious that in science, we value unique, creative thinkers, but we teach scientists to progress in a formulaic manner that rarely takes each person's individual strengths into account. Surprisingly, when we break the mold, we are often rewarded for it. This cycle of learning to survive using conventional wisdom but being rewarded for a unique path outside of it seems to be an unspoken key to success. I am honored to be awarded the 2020 Women in Cell Biology Junior Award for Excellence in Research and am thrilled to share some of the unconventional guiding principles that brought me to where I am in this rich scientific landscape. The game changers in the early phase of my career were informal mentors, open scientific communication, and persistence in pursuing difficult scientific questions.**

INSPIRATION FROM STRANGERS

I recall as a child thinking that if I could better understand those I admired, I might grow to naturally develop their positive attributes. It turns out this philosophy has served me well throughout my life. Like many, my first scientific heroes came from reading the literature and being inspired by their work. However, after starting my postdoc, I started becoming inspired by scientists outside my field through their writings on science blogs and on Twitter (Claus Wilke, Matt Might, Radhika Nagpal, Mike Eisen, Drug Monkey, Darren Boehning, Mike Nitabach, Jason Rasgon, Casey Greene, and many more). This might sound unusual, but lurking around frank discussions about science online between people I didn't know has strongly influenced my philosophy on how I do science, pursue funding, and run a laboratory. I now try to pay it forward by sharing things I have learned on my blog and on Twitter.

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PREPRINTS

I started my laboratory in 2015 at the University of Kansas Medical Center (I have since moved to the Geisel School of Medicine at Dartmouth). At that time, preprints, which are manuscripts posted online before peer review, were becoming more prevalent in the biosciences, with BioRxiv founded in 2013. I am thankful organizers made the first meeting of Accelerating Science and Publication in Biology (ASAPbio), an organization pursuing transparency and innovation in publishing, available to view free online. I watched this meeting from home and it completely changed the way I do science. Having just started my lab, for the first time I would be primarily responsible for deciding how and where to publish. I decided then that all of our work would be preprinted. Further, I decided we would post our manuscripts online ahead of conferences, where those who really cared about our work would visit our posters and read our preprints. We could then use that feedback to improve our manuscripts before sending them to journals. I think we are still among the minority that follows this pipeline, but we continue to do so, largely because of the success we had the first time. We got outstanding feedback at a large conference where people not only could see our data on a poster, but also were able to analyze them in full. Incorporating this feedback before journal submission resulted in a smooth journal review process with no surprises. I was sold on preprinting and would never return to previous ways.

PEER MENTORSHIP

About a year into my first faculty position, I realized that many of the challenges I was facing were not new and were likely shared by all new faculty (what to order, who to hire, how to navigate funding, tenure, and much more). Why reinvent the wheel? And why not

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Abbreviations used: ASAPbio, Accelerating Science and Publication in Biology; UCSF, University of California San Francisco; PI, principal investigator.

learn from others' mistakes without relying too heavily on one or two people with limited experience? I had recently started my own laboratory Slack (a popular online messaging platform) to stay in quick communication with laboratory members and found it very easy to navigate. Why couldn't we have such a platform for new principal investigators (PIs) across the country/world and help each other? So I started New PI Slack, wrote a blog post about why I did it, and tweeted about it so that others could join. At 2000+ worldwide members later, along with a slew of offshoots for postdoc, student, model organism communities and beyond, it turns out I was not the only one that needed this! A great deal of effort by institutions goes into formal mentorship structures for faculty and students, but over the years, I have received the vast majority of feedback and guidance from ideal informal mentors unrestricted by geography, tailored for very specific aspects of my professional development.

NOT BEING OBSESSED WITH THE ACADEMIC GAME

I would say one of the most important things I did as an early career faculty member was listening to people who were not trying to be savvy and game the academic system to get promoted. I reasoned that if I changed everything about who I was and what I thought was important in order to get tenure, I might not want to be stuck with the person and scientist I had become. Instead, I spent time with people who had other aspirations. Some were doing science they thought was more exciting than safe. Others were trying to fight inequities in the system. Some were changing how we thought about publishing and evaluation. In every case, they taught me to shed fear and do my job exactly as I wanted to do it. I promised myself that I would pursue the science I loved and build a version of the job that was worth fighting for tenure to keep. For me, this still means that grants and manuscripts are atop my priority list whenever they are on my desk. However, it also means I say yes to advocacy roles that are important to me. The big surprise was that my other passions often synergize with my science and career advancement (through increased collaborations, speaking invitations, recruitment to my lab and more) rather than detracting from them.

DOING THE SCIENCE YOU LOVE

I often preach to students about being open-minded about their research interests, because I believe that scientists, curious by nature, can become interested in and obsessed with any kind of problem in science. That said, I have always been a cell biologist, long before I really understood what cell biology was. If I started over in science 1000 times, 999 of those times, I think I would end up studying the cytoskeleton. As a graduate student at the University of Utah in Wolfgang Baehr's lab, I studied trafficking through photoreceptor cilia in mice (Avasthi *et al.*, 2009, 2013; Ying *et al.*, 2014) and realized through my reading that so many of the fundamental discoveries in this field were made in the unicellular green alga *Chlamydomonas*. The idea of working in a model system that allowed mechanistic analyses and discovery of new regulatory pathways was extremely appealing, particularly a system so well suited to biochemical and genetic approaches. I joined the laboratory of Wallace Marshall at University of California San Francisco (UCSF), largely because he was incredibly creative, had a palpable excitement for science, and members of his lab were working in whichever model system they felt was most appropriate for their scientific questions. In Wallace's lab, I used chemical screening to identify many novel pathways regulating cilia (Avasthi *et al.*, 2012) but landed indirectly on a puzzling finding that few in the field seemed convinced by: that the actin cytoskeleton seemed to regulate the assembly of the ciliary microtubule superstructure in *Chlamydomonas* (Avasthi *et al.*, 2014), something that Bill Dentler had suggested decades earlier (Dentler and Adams, 1992). I was working on this problem for more than six months before I showed Wallace a key result that persuaded him that I might be on to something. I will always be grateful to him for giving me so much leeway to pursue a result he may have been initially skeptical about. Despite actin's role in many fundamental cellular processes, it took many more years, several more papers from my independent laboratory, and beautiful work from my brilliant colleague Masa Onishi (Onishi *et al.*, 2016, 2018, 2020) in the laboratory of John Pringle and in collaboration with Fred Cross to convince others in our field of actin's functions in *Chlamydomonas* ciliary assembly. We first had to lay the groundwork by studying fundamentals of actin biology in this alga. We did this in my lab via some brute-force trial and error and traditional cell biological approaches, but also by collaborating with experts in in situ cryo–electron tomography (former Marshall Lab baymate Ben Engel) and in actin biochemistry (collaborator and informal advisor David Kovar; Christensen *et al.*, 2019; Craig *et al.*, 2019; Jack *et al.*, 2019).

NOT LETTING OTHERS DICTATE YOUR VALUE

Throughout my short career, I have been very fortunate to have mentors in my life who believed in me and strangers who inspired me by their example. I have had amazing students and postdocs in the laboratory who have brought to our science their hard work and creativity. I continue to be humbled that they have trusted me with their careers. I have also learned that when you have goals including but not limited to science itself, it can be easy to get pigeon-holed as someone who is not serious about their work. Sometimes, I think it would be harder to question my dedication to my research if my hobbies were skiing or hiking, instead of getting into arguments in board rooms, in decision rooms, and on Twitter about creating better scientific practices. To all of you young scientists, I urge you to free yourself of others' expectations. This is difficult in a system that has such structured metrics for advancement, but those expectations cannot accommodate your spirit and ambitions. Write your own story, be bold, pursue the scientific questions that excite you, and know there are many paths to success and happiness in science!

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