

Building a path in cell biology

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ABSTRACT Setting up a new lab is an exciting but challenging prospect. We discuss our experiences in finding a path to tackle some of the key current questions in cell biology and the hurdles that we have encountered along the way.

We were both fortunate to receive the ASCB Early Career Life Scientist Award this year and were offered this opportunity to discuss our science and experiences. As we are at very similar stages in our careers (Iain has had a lab for 5 years, and Gia has had a lab for 6 years), we decided to compare our experiences starting our labs and conducting science and to discuss the decisions that we have made along the way.

WHAT IS THE PRIMARY GOAL OF YOUR RESEARCH?

Gia: We are trying to understand how the structure of the endoplasmic reticulum (ER) is generated and maintained. The ER is a massive organelle with an elaborate and dynamic shape. We have been studying how membrane-shaping proteins and interactions with the cytoskeleton generate the structure of this complex



G. Voeltz

organelle. To do this, we use an in vitro ER formation assay, electron microscopy (EM) tomography, and live-cell imaging to analyze the role of various factors on ER shape and dynamics at high resolution over time. In the past few years, we have become increasingly focused on the relatively nontraditional role of the ER in regulating the structure of other organelles with which it forms stable contact sites. We would like to understand how and why the ER is tethered to almost all other organelles.



I. Cheeseman

Iain: Our lab is focused on understanding the process of chromosome segregation during cell division. In particular, we are interested in how the kinetochore acts to connect chromosomal DNA to microtubule polymers from the mitotic spindle. To me, the kinetochore is the most fascinating mo-

lecular machine in a cell, with key structural requirements, the ability to generate force, and a tight regulation to control and coordinate its activities. In recent years, there has been an explosion in the identification of kinetochore proteins. However, the molecular mechanisms that allow the kinetochore to contact DNA, direct assembly of the kinetochore, regulate kinetochore function, and facilitate interactions with microtubules (as well as many other important activities) remain ill-defined. Our lab is taking combined cell biological, biochemical, structural, and proteomic approaches to address these questions. I think that this is an incredibly exciting time in the mitosis field, with the possibility of finally being able to generate detailed molecular explanations for processes people have been looking at down the microscope for more than 100 years.

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Abbreviations used: EM, electron microscopy; ER, endoplasmic reticulum; PI, principal investigator.

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DESCRIBE YOUR RESEARCH GROUP

Gia: I have a small lab. Over the past several years I have typically had three to four PhD students, an EM technician, a standard technician, and two to three undergraduate students. All my PhD students supervise undergraduates, and some even end up with their own technicians, who are typically talented undergraduates from my lab who have recently graduated and want to go on to graduate school in the future. I like this model, because these “teams” can be really productive, and the PhD students learn a lot about supervising. Because my lab is so small, I can have only about four projects going on at one time, but I am able to think about these projects constantly, and this helps to keep them on track.

Iain: Our lab is also of a small to intermediate size (currently two postdocs, four graduate students, and a graduate student-like technician). I like this size. I would ideally prefer to have a lab of eight to twelve people, so I could be involved with the work that everyone is doing but also continue to do at least some bench work myself. Our lab is an incredible group of smart, talented, and hardworking people. I feel as though my primary job is to make sure that there are no barriers between them and the science they want to do.

WHAT IS THE BEST PART OF YOUR JOB?

Gia: I think the best part of being a scientist is discovering something new but also overcoming challenges both scientifically and professionally by persevering. I like what I do but not always, and that is okay. I don't like it when my papers get rejected, or a grant goes unscored. But sometimes our papers do get accepted, and my grants do get funded, or an idea comes to fruition, and those days are such great days. The other best part is training students to become scientists. Yesterday, I looked around my lab, and I thought about how much I really liked and respected everyone there and how lucky I was to be in a position to guide this amazing group of people. I have had great mentors, and I like to pass on what I've learned from them.

Iain: I enjoy getting to live vicariously through the science that is happening in our lab. There are so many cool things still to discover. I like the day-to-day process of science. I still get excited when someone gets their cloning to work, let alone when they find something fundamentally new. I have really loved seeing what the people in our lab have accomplished, including new directions and ideas that I never would have thought we would be working on, and new approaches that I wouldn't have thought we would be able to apply. I have a lot of respect for the people in our lab. It is really a pleasure to come in every day, and I look forward to seeing what we will do tomorrow.

WHAT HAS BEEN THE BIGGEST CHALLENGE OF BEING AN ASSISTANT PROFESSOR?

Gia: Teaching a large undergraduate class: Cell Biology with ~200 students. I thought I would be good at this, but I underestimated the task and struggled my first year. It's been 5 years now, and I think that I have got it down, but I have had to work really hard at it, and I still always overprepare for lecture. What was initially my biggest challenge has become an invaluable opportunity to contribute to the science education of so many and to be able get the students excited about cell biology. Now I enjoy this course immensely and have even discovered a surprising benefit: this class has influenced my research program. For example, we started to study organelle dynamics on microtubules as a direct result of my teaching a section on the cytoskeleton.

Iain: I feel as though I have a new and different answer to this question every 2 months. It is a great job, because there are always new challenges, but I am also sure that I will never feel as though I am completely comfortable with each of these challenges (starting things up, recruiting new people, getting funding, publishing, teaching, etc.). For me, both my graduate and my postdoc work involved a very steep learning curve as I learned new concepts and approaches, but this curve began to level off at the end of each experience. I feel as though the learning curve as a principal investigator (PI) just continues upward, which is complicated, but it is also nice that there is always something new to learn.

WHAT DID YOU LEARN FROM YOUR MENTORS THAT HAS HELPED YOU THE MOST?

Gia: My PhD advisor, Joan Steitz, expected us to always be prepared. We were expected to know the background, details, and rationale of an experiment and to be able to explain it clearly to others. I try to be prepared and never procrastinate in order to make every situation a little less stressful; for example, I will typically have a talk ready a solid week before I present it. The most useful thing that I learned from my postdoctoral advisor was to seize the moment and make time for the things that are truly important. If I were in Tom Rapoport's office discussing my project, and he thought one of his colleagues might have a useful suggestion, he would literally jump out of his seat at that very moment and drag me across campus to see whether that colleague was available. He always had time to talk about science or to work on a paper, and I try to do the same.

Iain: I had two very different sets of mentors as a graduate student and as a postdoc. For my graduate work, I was in a more senior lab with ~25 people and two PIs (David Drubin and Georjana Barnes). For my postdoctoral work, I was in a brand-new lab (Arshad Desai and Karen Oegema). I showed up about 2 weeks after Arshad and Karen, although their lab grew quickly from there. During both my graduate and postdoctoral work, I watched these PIs to see how they were running things and the decisions that they were making. I have tried to combine their different approaches as much as possible in a way that feels right to me. There were two things in particular that my previous mentors did that I really appreciated. First, they did a great job of creating a context in which good science could happen. There are a number of things that you need to be successful as a graduate student or postdoc, including funding, a critical mass of other good and constructive people in the lab, access to equipment and reagents, collaborators, the ability to efficiently publish your work, and PIs who do their best to ensure the future success of people from the lab. We sometimes take these things for granted, but I now realize how much work happens behind the scenes to make this a reality. Second, I really enjoyed being able to discuss science with my previous mentors. It is nice to have someone to bounce ideas off and to argue with about big picture questions and ideas.

WHAT ADVICE DO YOU HAVE FOR OTHER PEOPLE JUST STARTING OUT?

Gia: That you don't need to be good at everything from the very beginning. When I was a student, I ran beautiful gels and worked really hard, but I didn't know how to form hypotheses. After my PhD work, I started all over in a new field, and it was a challenge to catch up, but it was worth it. Even as a postdoc, I was not a great writer or a natural speaker. My mentors are great speakers and writers, and by watching them and others, I learned. These skills can come with

experience, and so my advice is that you should work on one thing at a time until you get better at it.

Iain: I make a lot of mistakes. Overall, I'm okay with this, as long as I can continue to learn from the things that I have messed up. It is important to realize that everyone starting a new lab struggles with things. In addition to turning to more senior colleagues for advice, I think that it is helpful and fun to have a network of other junior faculty who can let you know that everyone struggles now and then, and who give one another advice on how they handled the new challenges (teaching for the first time, hiring new people, etc.). In addition, go with your gut. If you don't feel excited or passionate about a research direction or hiring someone into your lab, it is probably not the right decision.

WHAT IS YOUR LIFE LIKE OUTSIDE OF LAB?

Gia: I am a soccer mom. Our two kids now have soccer practice or games 5 days a week. I love it. We also have a ski resort less than an hour away, so we ski almost every weekend in winter: my kids are only five and nine, but they are already great skiers, which is really fun. My husband Brian is also a scientist, and it's great that we can give each other advice about our research. I have also begun to travel a lot in the past few years to give seminars about our research

at conferences and universities; this is absolutely one of my favorite parts of what I do.

Iain: My wife is a scientist at a biotech company in Cambridge. We met our first day of graduate school, and making sure that both of us can be happy with our scientific careers has always been an important challenge. It has been wonderful to have a partner who understands my ups and downs in science, and who is such a good source of input, advice, and ideas. Since we arrived in Boston, our lives have changed a lot. We now have two daughters (4 years old and 1 year old), who are awesome. Although this has made a number of aspects of life much more complicated, it is really nice to have this balance. I love being in lab, and then I love going home to be with my family.

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