Reflections on mentorship as an early career researcher

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ABSTRACT **It is my great honor to receive the 2022 Günter Blobel Early Career Award from the American Society for Cell Biology. Reflecting upon my research and career trajectory, I recognize the incredible support of my mentors and the hard work of everyone within my lab. I have always relied on a network of advisors and colleagues who supported me throughout my scientific journey. To better support my own trainees, I endeavor to pass on lessons learned while continuously developing and strengthening my own leadership potential. I am a relentless advocate for the success of my trainees, a legacy I pass on from my own mentors.**

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THE INDELIBLE MARKINGS OF EARLY MENTORSHIP

The trajectory of my early research career was imprinted by former research mentors. My graduate training at Princeton proved especially formative. I vividly recall watching Nobel Laureate Dr. Eric Weischaus grow increasingly animated while describing his own career trajectory and passion for *Drosophila* development as he looped a time-lapse video of a gastrulating *Drosophila* embryo, culminating with him leaping on top of the conference table to the gasps and nervous laughter of my first-year graduate class. At this moment, I was drawn to the potential of microscopy, value of basic science, and power of committing to work that challenges and inspires. In a later discussion, it was Eric who guided me to complete a graduate rotation with Dr. Elizabeth (Liz) Gavis based on her lab's use of microscopy and her exemplary reputation as an experimentalist and mentor.

Dorothy A. Lerit

I credit much of my personal success in academia to my graduate training with Liz. As a graduate student in the Gavis lab, I was trained in how to conduct rigorous, impactful basic research. Moreover, I learned how to think like a scientist—to ask questions, form hypotheses, design experiments, collect data, and analyze results. I was trained to direct my own projects and develop new ones; in short, to think creatively and independently. While these skills attest to Liz's strength as a mentor, features that truly set Liz apart include her ability to set a consistent tone in her laboratory, one that is both congenial and professional, where people work to the highest standards, push themselves to work harder and smarter, and still love to come to work every day. Another key skill I credit directly to Liz is her training in how to "tell a story." Liz is exceptionally rigorous in providing constructive feedback on oral presentations and manuscript drafts. She is precise and effective. Since establishing my independent group at Emory, I have tried to mirror Liz as I consider the lab atmosphere I wish to nurture and the mentorship I provide my own trainees. Weekly one-on-one and group meetings, expedient and constructive feedback on written texts, purposeful practice talks, an emphasis on research progress over specific lab hours, and engagement at seminars, department events, and scientific conferences are all cornerstones of my graduate training experience and now features of my own research group.

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Abbreviations used: Ana2, anastral spindle 2; ASCB, American Society for Cell Biology; EMBO, European Molecular Biology Organization; NIH, National Institutes of Health; Plk4, polo-like kinase 4; PLP, pericentin-like protein.

Part of the strength of Liz's approach to successful mentoring is her measured touch. She treats her personnel or colleagues with courtesy and fairness. Similarly, the mentee–mentor expectations in my lab include professionalism, respect, and effective communication.

Liz was and continues to be an exceptional role model. When I started graduate school, I already knew I wanted a research career. However, there were moments of heightened anxiety when I questioned whether I could successfully compete for an academic position. I discussed my concerns with Liz, who encouraged me to pursue my goal.

Now, through my varied roles in mentorship and teaching, I observe pervasive imposter syndrome among graduate students (Pederson, 2020). When I meet with new students, I always ask them whether they've considered their career goals. The handful interested in an academic career invariably express self-doubt. In these situations, I find myself marrying the mentorship styles of Liz with those of my postdoctoral advisor, Dr. Nasser Rusan, who is both direct and goal oriented. I encourage students to follow their ambition, discuss benchmarks of success, and motivate them to persevere.

FOLLOWING THE SCIENCE

As an incoming graduate student, I had a narrow view of what I wanted to study based on my sole previous undergraduate research. My first project was characterized by exciting early discoveries, followed by frustration. The mutants we were using were original lines from classic maternal-effect screens (Schupbach and Wieschaus, 1989), but we identified second-site mutations obfuscating some of our results. Although we obtained new alleles, Liz and I agreed to prioritize another project, which was quickly gaining momentum. Like many imaging-intensive projects, this meant working late into the night to capitalize on open microscope core time. My last two years of graduate training were my most productive. I learned that changing course can allow for progress and when things are working in the lab, it's best to keep going.

My research used live imaging to uncover how germline determinants are incorporated into the germline and segregated from the soma to ensure proper cell fate specification. I found that the maternally provided RNAs and proteins, which define the germ plasm and instruct germline fate, do not stay anchored to the posterior cortex; rather, they dissociate and undergo directed, dynein-dependent trafficking along microtubules to accumulate around proximal centrosomes (Lerit and Gavis, 2011).

As the project progressed, I contacted centrosome researchers and became entrenched in centrosome literature. I was fascinated by how the organelle breaks the symmetry of polarized cells and aligns the mitotic division axis. Reaching out to centrosome leaders forged a growing network in my newly chosen field and helped connect me to my future postdoc advisor, Nasser.

For personal reasons, my postdoc search was geographically restricted, and the National Institutes of Health (NIH) stood out as an excellent option. I was Nasser's first postdoctoral hire at the NIH, and it was he who introduced me to the American Society for Cell Biology (ASCB). Nasser was an ASCB lifer and an intrepid cell biologist who refined my focus on microscopy and quantitative analysis, while introducing me to thought leaders in the centrosome field, among other rock star cell biologists.

Nasser's young and untenured government lab offered a contrasting view to my graduate experience—a transition facilitated by the community of postdoctoral researchers within our center. While Nasser had no shortage of research ideas or enthusiasm, he insisted that I spend the first few weeks deeply engaging with the literature. He also emphasized project planning and management, which helped me make rapid progress. Nasser's penchant for storyboarding nascent ideas grew into my own current emphasis on outlines, along with the conviction that it's never too early to start assembling manuscript figures.

The pace in Nasser's lab was swift. Within two years, we submitted our first manuscript, and another one year later. I learned how to rapidly organize and complete projects, an invaluable skill for a future principal investigator establishing her independent lab.

Nasser was curious about pericentrin-like protein (PLP), a conserved component important for pericentriolar material organization within asymmetrically dividing neural stem cells (Martinez-Campos *et al.*, 2004). Curiously, the phenotype of *plp* mutants varied throughout the cell cycle, and we wanted to understand why.

Nasser had recently completed his postdoctoral training with Dr. Mark Peifer at UNC Chapel Hill, someone who would soon influence my own career. In Mark's lab, Nasser discovered that the duplicated centrosomes within interphase neural stem cells show marked asymmetries in maturation, the process by which centrosomes recruit additional pericentriolar material required for microtubule organization and spindle formation (Gould and Borisy, 1977; Khodjakov and Rieder, 1999). During late interphase, one of the duplicated centrosomes in neural stem cells is transiently inactivated until mitotic onset, while the other centrosome remains active as a microtubule-organizing center (Rusan and Peifer, 2007).

I discovered that PLP is required for the transient inactivation of the basal-fated centrosome during interphase. Loss of *plp* produced two active centrosomes, leading to centrosome segregation errors and multipolar spindles (Lerit and Rusan, 2013). My first ASCB oral presentation was actually a talk on this project slated for Nasser, who offered the opportunity to me. I was deeply grateful that he sacrificed the opportunity for my benefit, even casually chatting with me before my presentation to keep my nerves in check.

In a recent conversation with Liz, she mentioned that part of our job as mentors is to self-sacrifice for the benefit of our trainees, whether it's a project a departing trainee wants to take or an opportunity to gain visibility. You know you're doing it right, she noted, if it hurts a little bit.

FINDING MY NICHE

I met Mark Peifer at one of my first ASCB meetings. At each annual meeting, we chatted about my postdoc and plans for the future. After a few years, Mark bluntly asked why I was still working on PLP and provided advice: find what I do best, and do that. This simple statement gave voice to the idea that I had a future in cell biology research and valuable unique skills.

I found Mark's comment salient. One year into my postdoc, four research papers came out describing centrosome organization using structured illumination microscopy (Fu and Glover, 2012; Lawo *et al.*, 2012; Mennella *et al.*, 2012; Sonnen *et al.*, 2012). Two years later, at the EMBO Centrosomes and Spindle Pole Bodies conference in Portugal, several research groups presented work defining Ana2 as a substrate for Plk4-mediated phosphorylation required for procentriole formation, a finding confirmed by others (Dzhindzhev *et al.*, 2014; Ohta *et al.*, 2014; Arquint, Gabryjonczyk, Imsen, Bohm, *et al.*, 2015; Moyer, Clutario, *et al.*, 2015). While clearly these were seminal findings,

FIGURE 1: Photo of the Lerit lab taken in August 2022. From left to right, top row: Christian Husbands, Junnan Fang, Hala Zein-Sabatto, Joey Buehler, Jovan Brockett, and Advik Bharadwaj. Seated: Temitope Adebambo, Dorothy Lerit, Taylor Hailstock, and Weiyi (Rose) Tian. Photo credit: Dr. Joanna Wardwell-Ozgo.

I realized that I needed to find my own research niche, as I did not want to compete with the world's top centrosome labs studying similar research questions.

I recalled a landmark genome-wide screen for RNA localization patterns within early *Drosophila* embryos (Lecuyer *et al.*, 2007). Among the ~70% of localized mRNAs was a small subset that apparently localized near spindle poles. Now, I recognized that most of the spindle pole–localized mRNAs encoded proteins that also localized to centrosomes or functioned in spindle pole alignment. With this observation, I melded my unique experiences and personal interests in RNA localization and centrosome biology into what is now my independent research program.

My laboratory investigates centrosome-localizing mRNAs, a topic long ignored in the centrosome field due to confounding early reports (reviewed in Ryder and Lerit, 2018; Zein-Sabatto and Lerit, 2021; Lerit, 2022). We aim to define which RNAs localize to centrosomes, how they get there, and most importantly, their function. This work is based on a solid foundation of prior work demonstrating that mRNAs and ribosomes localize to centrosomes in diverse cell types. Our early work led to a pivotal contribution: the first direct evidence that RNA localization and on-site translational control contribute to centrosome functions, mitotic fidelity, and viability (Ryder, Fang and Lerit, 2020). Our work demanded a computational pipeline to quantitatively define RNA distributions at single molecule resolution, an effort spearheaded by my first postdoctoral fellow, Dr. Pearl Ryder (Ryder and Lerit, 2020). This open-source pipeline was adapted by others in the laboratory, including Dr. Junnan Fang, to examine other RNA distributions and contributions of conserved RNA-binding proteins to centrosome regulation and function (Fang and Lerit, 2022). In many respects, I feel that our work is only just begun.

I am incredibly proud of our diverse, creative, and hardworking team (Figure 1) and indebted to the efforts of my current and prior trainees. I try to instill in them the same philosophy I learned from another informal ASCB chat with Mark when I was stressed about addressing a manuscript revision. He noted that there is no point worrying about things beyond our immediate control, be it critical manuscript reviews, the uncertainty of the faculty job market, or tenure prospects. He looked at me and said, "just do good science."

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REFERENCES

Boldface names denote co–first authors.

Arquint C, Gabryjonczyk AM, Imseng S, Bohm R, Sauer E, Hiller S, Nigg EA, Maier T (2015). STIL binding to Polo-box 3 of PLK4 regulates centriole duplication. eLife 4, e07888.

Dzhindzhev NS, Tzolovsky G, Lipinszki Z, Schneider S, Lattao R, Fu J, Debski J, Dadlez M, Glover DM (2014). Plk4 phosphorylates Ana2 to trigger Sas6 recruitment and procentriole formation. Curr Biol 24, 2526–2532.

Fang J, Lerit DA (2022). Orb-dependent polyadenylation contributes to PLP expression and centrosome scaffold assembly. Development 149, dev200426.

Fu J, Glover DM (2012). Structured illumination of the interface between centriole and peri-centriolar material. Open Biol 2, 120104.

Gould RR, Borisy GG (1977). The pericentriolar material in Chinese hamster ovary cells nucleates microtubule formation. J Cell Biol 73, 601–615.

Khodjakov A, Rieder CL (1999). The sudden recruitment of gamma-tubulin to the centrosome at the onset of mitosis and its dynamic exchange throughout the cell cycle, do not require microtubules. J Cell Biol 146, 585–596.

Lawo S, Hasegan M, Gupta GD, Pelletier L (2012). Subdiffraction imaging of centrosomes reveals higher-order organizational features of pericentriolar material. Nat Cell Biol 14, 1148–1158.

Lecuyer E, Yoshida H, Parthasarathy N, Alm C, Babak T, Cerovina T, Hughes TR, Tomancak P, Krause HM (2007). Global analysis of mRNA localization reveals a prominent role in organizing cellular architecture and function. Cell 131, 174–187.

Lerit DA (2022). Signed, sealed, and delivered: RNA localization and translation at centrosomes. Mol Biol Cell 33, pe3.

Lerit DA, Gavis ER (2011). Transport of germ plasm on astral microtubules directs germ cell development in *Drosophila*. Curr Biol 21, 439–448.

Lerit DA, Rusan NM (2013). PLP inhibits the activity of interphase centrosomes to ensure their proper segregation in stem cells. J Cell Biol 202, 1013–1022.

Martinez-Campos M, Basto R, Baker J, Kernan M, Raff JW (2004). The *Drosophila* pericentrin-like protein is essential for cilia/flagella function, but appears to be dispensable for mitosis. J Cell Biol 165, 673–683.

Mennella V, Keszthelyi B, McDonald KL, Chhun B, Kan F, Rogers GC, Huang B, Agard DA (2012). Subdiffraction-resolution fluorescence microscopy reveals a domain of the centrosome critical for pericentriolar material organization. Nat Cell Biol 14, 1159–1168.

Moyer TC, Clutario KM, Lambrus BG, Daggubati V, Holland AJ (2015). Binding of STIL to Plk4 activates kinase activity to promote centriole assembly. J Cell Biol 209, 863–878.
Ohta M, Ashikawa T, Nozaki Y, Kozuka-Hata H, Goto H, Inagaki M, Oyama M, Kitagawa D (2014). Direct interaction of Plk4 with STIL ensures formation of a single procentriole per parental centriole. Nat Commun 5, 5267.
Pederson T (2020). A 20-year encounter with the imposter syndrome. Mol Biol Cell 31, 2509–2510.
Rusan NM, Peifer M (2007). A role for a novel centrosome cycle in asymmetric cell division. J Cell Biol 177, 13–20.
Ryder PV, Fang J, Lerit DA (2020). Centrocortin RNA localization to centrosomes is regulated by FMRP and facilitates error-free mitosis. J Cell Biol 219, e202004101.
Ryder PV, Lerit DA (2018). RNA localization regulates diverse and dynamic cellular processes. Traffic 19, 496–502.
Ryder PV, Lerit DA (2020). Quantitative analysis of subcellular distributions with an open-source, object-based tool. Biol Open 9, bio055228.
Schupbach T, Wieschaus E (1989). Female sterile mutations on the second chromosome of Drosophila melanogaster. I. Maternal effect mutations. Genetics 121, 101–117.
Sonnen KF, Schermelleh L, Leonhardt H, Nigg EA (2012). 3D-structured illumination microscopy provides novel insight into architecture of human centrosomes. Biol Open 1, 965–976.
Zein-Sabatto H, Lerit DA (2021). The identification and functional analysis of mRNA localizing to centrosomes. Front Cell Dev Biol 9, 782802.