Erin Goley: Catching the bug for studying the cytoskeleton

Marie Anne O'Donnell

Erin Goley investigates how the microbial cytoskeleton controls cell growth and division.

As a schoolkid in North Kingstown, RI, Erin Goley's stepdad helped her build "the coolest cell in the class" with clear, self-hardening resin encapsulating various objects representing parts of the cell within a fish bowl membrane. But this early foray into cytoskeletal research was sidelined as Goley instead enjoyed developing tools to monitor viral and fungal plant pathogens at the USDA laboratories during her time as an undergraduate at Hood College, Frederick, MD. Visiting the University of California, Berkeley, on a sunny February weekend convinced Goley to join their molecular and cell biology PhD program, where her rotations were mainly in laboratories studying the interactions of intracellular pathogens with host actin. Matt Welch's purification of Arp2/3 as the host factor that nucleates actin on the surface of *Listeria* is one of Goley's all-time favorite experiments: "I love the concept that intracellular pathogens are the best cell biologists around and that we can learn so much about fundamental cell biology by discovering how they manipulate it to their advantage." So Goley spent her postgraduate years in Welch's laboratory investigating the mechanisms of Arp2/3 activation (1) as well as baculovirus-induced actin rearrangements (2). As a card-carrying cell biologist, Goley was next drawn to the fledgling field of bacterial cell biology and brought her expertise in eukaryotic cytoskeletal biochemistry to studying the cytoskeleton of *Caulobacter crescentus* as a postdoctoral researcher with Lucy Shapiro at Stanford University. *Caulobacter* is famous for its dimorphic life cycle: it has two primary cell types, a motile form called the swarmer and a sessile form called the stalked cell, and it produces one of each through an obligate asymmetric cell division. In Shapiro's laboratory, Goley used *Caulobacter* as a model system to investigate the role of the conserved tubulin-like GTPase, FtsZ, in orchestrating bacterial division (3, 4). Shapiro gave Goley the support and intellectual freedom to pursue whatever questions inspired her "as long as it was in *Caulobacter*!" and Goley took her new favorite bug to Johns Hopkins University to establish her own research program tackling the question of how bacterial cell growth and division are controlled by FtsZ. We contacted her to learn more.

What first drew you to study the bacterial cytoskeleton?

At the time I was considering fields for postdoctoral study, in 2005, the bacterial cytoskeleton was a really new thing. MreB and FtsZ had only been demonstrated to be true homologues of actin and tubulin, respectively, when their structures were solved about five years prior. We knew, and still know, far less than for eukaryotic cytoskeletons about what these bacterial polymers really do, how their structures relate to their functions, or how they are regulated by interacting partners. I thought studying the bacterial cytoskeleton would marry my long-term interest in microbiology with the love for the cytoskeleton I acquired in graduate school, and I felt that the field was replete with fundamental mechanistic, and even phenomenological, questions. The stunning diversity observed in the cell biology of different bacteria, the dangerous rise in antibiotic resistance, and the importance of bacteria to human health both as pathogens and as integral components of our microbiota continue to affirm my original motivation to study fundamental aspects of bacterial cell biology.

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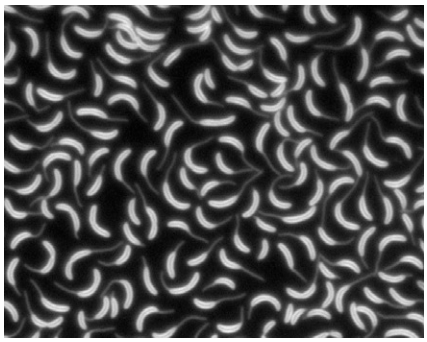
What is your laboratory actively working on?

When I started my laboratory at Hopkins, we were pretty focused on FtsZ and its direct regulators. During my postdoc, I had identified two new binding partners of FtsZ and we continued characterizing the interactions of those partners with FtsZ and their effects on the execution of division (5). We like to complement genetic and imaging approaches with in vitro biochemistry of purified components to come to a mechanistic understanding of the process, but we've been frustrated by a lack of robust in vitro assays for the physiologically relevant, membrane-associated form of FtsZ. To overcome that roadblock, we have recently put a lot of energy into establishing in vitro assays for monitoring FtsZ assembly, activity, and structure on membranes, and I'm really excited about our progress.

Erin Goley. PHOTO COURTESY OF ERIN GOLEY.

Another aspect of our research that's really taken off recently is investigating the link between FtsZ and cell wall remodeling. A few years ago, we were making variants of FtsZ to test the function of the intrinsically disordered linker between its polymerizing GTPase domain and the C-terminal peptide that binds membrane-anchoring proteins. It came as a complete surprise when we expressed a variant of FtsZ completely lacking the linker and found that it was lethal. The cells looked as if they had been treated with cell wall–targeting antibiotics like penicillin! It turned out that the FtsZ variant was leading to specific changes in cell wall chemistry, but without affecting the ability of FtsZ to recruit downstream

modonnell@rockefeller.edu



Fluorescence microscopy of *Caulobacter crescentus*.

proteins to the site of division (6). We hypothesized that, beyond just serving as a passive scaffold, FtsZ normally regulates specific cell wall enzymes in a linker-dependent manner. The linker mutant has become a really powerful tool that we are using to connect the dots from FtsZ to the cell wall. Coming into the field as a cytoskeletal biologist, I initially tried to focus just on the cytoplasmic side of things with FtsZ, but the bugs are telling us that the most important thing FtsZ is doing is influencing cell wall remodeling. Looking ahead, some of the forward genetics approaches we have used to address the FtsZ–cell wall connection are taking us into unexpected, but super exciting, new areas of global cell shape regulation and adaptations of growth in response to stress.

What kind of approach do you bring to your work?

Our general strategy is to hit a question with all of the experimental techniques available to us. In my laboratory that means we use imaging, genetics, biochemistry, and some genomics. I'm also a huge fan of collaboration to incorporate new or highly specialized approaches in the most efficient way possible. As we have begun to think more about the links between the cytoskeleton and cell wall, I'm also finding a lot of inspiration from work on cytoskeletal function in eukaryotic organisms with cell walls (i.e., plants and fungi). My favorite Gordon Research Conference of late is the plant and microbial cytoskeleton meeting, where you see these conceptual similarities echoed in the ways bacterial and eukaryotic walled organisms use their cytoskeletons to direct growth and division.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader?

I think I was well trained to do science, to be a mentor, to write, speak, and teach. Being a "boss" is something that didn't come naturally for me, though. It has been on-the-job training to learn how to motivate different trainees, some of whom really need and even want a PI who gives them strict deadlines and leans on them hard when they need to get things done.

"You can only control your own actions, not other people, so focus on what you can control and use that to make things happen."

What has been the biggest challenge in your career so far?

Learning to be resilient and not take rejections personally.

What is the best advice you have been given?

"There are two types of people, doers and people who aren't doers. You're a doer, so you just have to accept that you're going to be the one getting stuff done." This came from Matt [Welch] when I was in grad school. To me the broader message is that you can only control your own actions, not other people, so focus on what you can control and use that to make things happen.

What hobbies do you have?

My wife accuses me of being a serial hobbyist (the dusty ukulele and hula hoop in my basement are evidence in her favor), but one that I picked up in graduate school and still love is knitting. I've even knitted stuffed *Caulobacters*. Lately my biggest hobbies are my kids, though. My son Beck is 7 and daughter Remy is 2, and they keep us busy and laughing and grounded.

Any tips for a successful research career?

I think most important is choosing research advisors with whom you can have a productive and healthy working relationship. Ignoring red flags thinking your love of the scientific topic will overcome an iffy relationship with the mentor is a risky strategy. Your PhD and postdoc advisors will be some of your most important advocates for the duration of your career and you need them on your side. Matt [Welch] and Lucy [Shapiro] were both incredibly supportive advisors and continue to be the people I turn to first for advice.

Also incredibly important: Enjoy the journey. If you're only focused on the endpoints of getting the PhD, getting the job, etc., you'll be miserable. I loved graduate school, I loved my postdoc, and I love being a PI. They each have their high and low points, but how lucky am I to be able to make a living playing in the laboratory, asking the questions I find most interesting?

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Goley and family.