Margot Quinlan: Muscling in on oogenesis

Marie Anne O'Donnell

Quinlan investigates how the cytoskeleton polarizes oocytes.

Margot Quinlan's family moved from Brooklyn, NY, to the San Diego area, which was a culture shock for the 10 year old at the time. However, Quinlan stayed on the West Coast and took a year out from studying as an undergraduate at Reed College in Portland, OR, to work with Rick Leiber at the University of California, San Diego (UCSD), who first introduced her to the cytoskeleton and its role in muscle physiology. Upon returning to Reed College, Quinlan performed her senior thesis project off campus with Jon Abramson at Portland State University, again studying the biophysical and cell biological regulation of muscle tissue. But Quinlan wanted to travel before going to graduate school and ended up working with the cardiovascular researcher Friedrich Luft at the Universitat Erlangen-Nurnberg for two years. Upon returning to the US, Quinlan investigated how myosin motor proteins control contractility in the cytoskeleton as a graduate student in Yale Goldman's laboratory at the University of Pennsylvania (1).

Understanding the ability of the force-generating myosins to control the cytoskeleton in such molecular depth inspired Quinlan to find out how other proteins regulate the actin cytoskeleton. As a postdoc in Dyche Mullins' laboratory at the University of California, San Francisco, Quinlan discovered that the *Drosophila melanogaster* polarity factor Spire was a new type of actin nucleator (2). Together with the formin Cappuccino, Spire is required for the formation of an actin mesh in *Drosophila* oocytes and the polarization of these cells (3). It was unclear why two proteins with a similar function are necessary to build this actin mesh but Quinlan found that Spire and Cappuccino bind directly to each other and this interaction is critical for oogenesis in *Drosophila* (3–5). Despite enjoying these research experiences in laboratories throughout the US and Germany, Quinlan considers California home and set up her own laboratory at UCLA in 2008 to study how the cytoskeleton regulates cell polarity.

Quinlan's laboratory is currently figuring out how Spire and Cappuccino work together to build the actin mesh in oocytes in vivo and how the two proteins synergistically control actin assembly at the molecular level in vitro. Disassembly of this actin mesh precedes the onset of "cytoplasmic streaming" in oocytes, a process in which the movement of microtubules has a dramatic effect on the fluid behavior of the oocyte cytoplasm (6). Quinlan's team is investigating how changes in the regulation of Spire and Cappuccino reorganize the cytoskeleton to drive this cytoplasmic streaming process and how the timing and functional effects of cytoplasmic streaming control polarization of the oocyte. Mammals have homologues of Spire and Cappuccino that build an analogous actin mesh in their oocytes. They are also expressed in epithelia and neurons—cells that are notable for their ability to establish polarity like oocytes.

We contacted her to learn more.

"No one ever described having a lab as running a small business but that's what it is."

When did your interest in science begin?

I have a hard time remembering any specific events surrounding my becoming interested in science. I never pulled the wings off of bugs or anything like that when I was a kid. I think my mother knew before I did that I wanted to major in biology. However, I took a year off in the middle of college and had the good fortune to work for Rick Lieber at UCSD. Rick was an amazing role model who truly loved his job. I think he was excited to have a student who wanted to become a scientist. He gave me so many opportunities, including independent projects and trips to conferences. Rick studied muscle physiology and started me on the path to loving the cytoskeleton. I can't tell you how many ways he influenced me and how lucky I was to have that opportunity.

Margot Quinlan. PHOTO COURTESY OF MARGOT QUINLAN.

What drew you to study the cytoskeleton?

I started in the muscle research field and then learned about the wide world of the cytoskeleton from Mark Mooseker (who discovered the superfamily of myosin motor proteins [7]), when he directed the Physiology course at the Marine Biology Lab in Woods Hole. That was a life changing experience! In Yale Goldman's laboratory I studied myosin because I arrived with ideas about muscle. I got him to work on myosin V before I left! It wasn't a long leap to actin and it was an exciting time in the cytoskeleton field, with the recent discovery of the Arp2/3 complex and formins happening while I was looking for a postdoc position. Some good luck and the opportunity to learn many new things led me through my postdoc to where I am now.

What are you currently working on?

I still think about actin all the time. The mechanisms of nucleation and building complex actin-based structures are fascinating. My focus is on the actin nucleators that are essential for polarity determination in the oocyte. In flies, there is an intriguing actin mesh that forms during oogenesis that we know very little about. It is dynamic, is essential for polarity establishment, in part by helping to organize microtubules, and prevents very cool fluid flows called microtubule-dependent fast cytoplasmic streaming (see *Drosophila* oocytes image below). I think there is much more to it, though and am working on figuring it out.

modonnell@rockefeller.edu

Quinlan laboratory 1.0. Photo taken in 2012. This was the core of the Quinlan group for the first six years, including the first students and postdoc. PHOTO COURTESY OF MARGOT QUINLAN.

What kind of approach do you bring to your work?

Rick Lieber once told me that you can be a "technique" person or a "question" person. That stuck with me. I am most definitely a question person and my approach is by "any means necessary." It's fun. It means learning new things often.

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

No one ever described having a laboratory as running a small business but that's what it is. It's an incredible responsibility having trainees and having to raise funds to pay them. I love it and lose sleep over it.

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

Every step feels like an important accomplishment: getting my PhD, discovering a new class of actin nucleators and interesting interactions between nucleators, getting a job, getting tenure. There was a point last year when I learned I got tenure and that my R01 grant had been renewed. That felt like success. That said, two really happy days stand out for me: the day my first postdoc got a great job and the day my first graduate students graduated.

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

Scientifically: I spent about two years hitting my head against a wall in a small dark room we called the nano-cave. Surface chemistry slowed my PhD progress. To this day, knowing when you are cutting your losses versus throwing in the towel on a project is a concept I struggle with. I'm sure I'm not alone there. Personally: starting a family. I waited until I was older to have a child. It was a very rough road but, fortunately, with a happy ending for us.

Who were key influences early in your career?

In addition to having some great mentors, I had the good fortune of getting my PhD at the University of Pennsylvania, where there was no lack of female role models. I remember being tongue-tied the first time I met Clara Franzini-Armstrong, as I had cited her work many times in my undergraduate thesis. I loved Actin Journal Club with Vivian Nachmias and Sally Zigmond. Anne-Marie Weber was a wonderful force of nature. It was also important to watch Erika Holzbaur navigate the scientific world as a junior faculty member back then.

"Know when you are cutting your losses versus throwing in the towel on a project."

What is the best advice you have been given?

"Don't be afraid to ask for help."

What hobbies do you have?

I had hobbies before I became a mother. I was a cyclist and did pottery. Pottery got me through grad school. I loved getting dirty, using my hands, and creating fun and functional art. I'll get back to them or pick up something new, in time. My daughter is four years old right now.

What do you think you would be if you were not a scientist?

I have often thought about this and never come up with a practical answer, which may explain why I am a scientist. I do remember wanting bankers' hours during some challenging times but I didn't actually want to be a banker. I used to joke that I could have been a travel agent because I loved planning trips. The internet took that opportunity away.

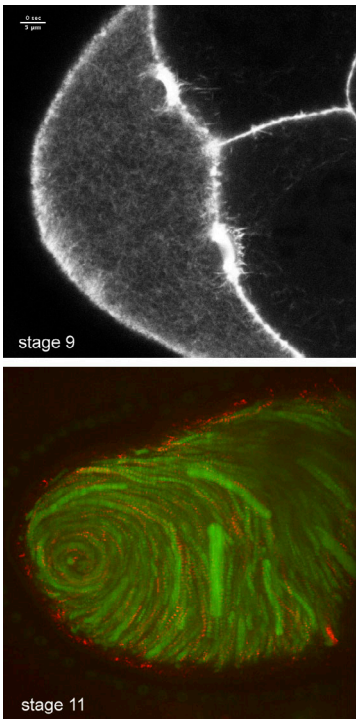
What has been your biggest accomplishment outside of the laboratory?

Riding my bicycle half way around France with a good friend is one accomplishment I will always cherish.

Any tips for a successful research career?

The work–life balance is not something you achieve, it's something you continually strive for. That said, you have to love science to do this job because you will be living it.

1. Forkey, J.N., et al. 2003. *Nature.* 422:399–404.
2. Quinlan, M.E., et al. 2005. *Nature.* 433:382–388.
3. Quinlan, M.E. 2013. *Development.* 140:4417–4425.
4. Vizcarra, C.L., et al. 2011. *Proc. Natl. Acad. Sci. USA.* 108:11884–11889.
5. Quinlan, M.E., et al. 2007. *J. Cell Biol.* 179:117–128.
6. Quinlan, M.E. 2016. *Annu. Rev. Cell Dev. Biol.* 32:173–195.
7. Mooseker, M.S., and R.E. Cheney. 1995. *Annu. Rev. Cell Dev. Biol.* 11:633–675.



Drosophila oocytes. (Top) The actin mesh. A stage 9 oocyte expressing Bill Bement's UtrnCH-GFP, the actin binding calponin homology domain of utrophin, which labels filamentous actin, reveals the actin mesh in a living cell. (Bottom) Fast streaming: A time-lapse projection of a stage 11 oocyte injected with fluorescein, which labels yolk granules, and red fluorescent beads (image acquired by students in the Molecular Biology Laboratory Physiology course in 2008). IMAGES COURTESY OF MARGOT QUINLAN.