# Rebecca Heald: Passionate about cycles

Rebecca Heald uses cutting-edge microscopy techniques to explore the cytoskeletal dynamics of cell division.

When she isn't cycling up a mountain, Rebecca Heald is blazing new trails in cell biology. Her work on dynamic cytoskeletal structures involved in mitosis and meiosis—particularly the microtubule-based mitotic spindle—has continually set the pace in her field.

After completing her graduate studies on nuclear lamins in Frank McKeon's laboratory at Harvard (1), Heald sought a change of scenery and research project. She moved to Germany where she joined Eric Karsenti in pursuing the mysteries of the microtubule cytoskeleton. A fortuitous collaboration led Rebecca to make a breakthrough in the field of spindle biology: DNA alone can nucleate the formation of a bipolar mitotic spindle apparatus (2).

**"An important thing for success is to figure out where your aptitude lies."**

Since returning to the United States, Heald and her many collaborators at the University of California, Berkeley, have continued to probe the mysteries of the mitotic spindle (3–5). She's a tough person to catch, but she slowed her pace long enough to discuss her experiences with us.

## GIVE ME A MOUNTAIN

***What are you most passionate about?***

In addition to the obvious things like chocolate and margaritas, I would have to say I'm passionate about cycling and microscopy.

***What makes you passionate about cycling?***

Cycling's something I have loved for a long time, but it wasn't until I was coming up for tenure that I got back into it seriously. And that was really because of my husband, who shares the cycling passion. He's a good influence on me.

It's great to have something to focus on outside of science, and cycling is now a very important aspect of my life. I love having a recreation that really challenges me, and that's so different from my work. You go to beautiful places, you test your limits, you're under your own power and it feels great.

***Do you cycle competitively?***

No, I don't like to crash, so I don't race. But I have done some pretty big rides. I did the Raid of the Pyrenees, which is cycling from the Atlantic to the Mediterranean through the Pyrenees in 100 hours. You go over something like 20 mountain passes, some of them as high as 2,115 meters. That was probably my biggest non-science accomplishment. Also that year, I rode the Everest Challenge, in which you climb the equivalent of Mount Everest—35,000 vertical feet in about 200 miles—over two days.

***Climbing mountains sounds tough.***

I love to climb mountains on my bike—and it is hard. You know, as you age you get more physical problems as things start falling apart on you, but you also gain some mental fortitude and determination. So overall, I'm a much better athlete now than I was when I was 20. It's one of the perks of getting older.

## TURNING POINT

***That kind of determination can come in handy in science, too.***

You have to be driven, for sure. You have to have some element of competitiveness—which most of us nice people try to suppress—but you have to get that grant, and to do that you have to have an edge.

I think a more important thing for success is to figure out where your aptitude lies. Do you enjoy sitting in front of a microscope? Do you enjoy sitting in front of a spectrophotometer? If you're lucky, you eventually figure out what you enjoy, and then you can start developing your niche.

Rebecca Heald

***When did you discover your niche?***

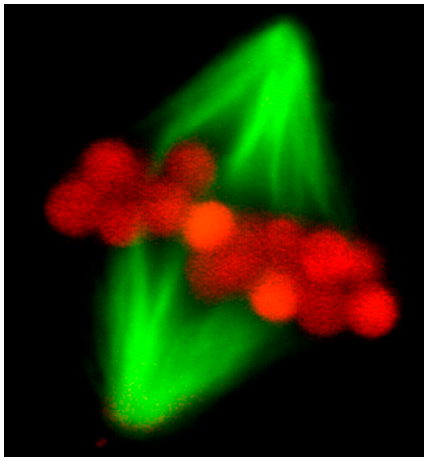
It evolved throughout graduate school and my post-doc. I've always been interested in dynamic cell structures, and their morphogenesis. As a graduate student I discovered microscopy, and loved it. I had been using it to study nuclear lamins, which are intermediate filaments. They have some dynamic behaviors, but they're not as dynamic as other cytoskeletal proteins. Microtubules are really the ultimate dynamic cytoskeletal element. So, for my post-doc I decided that I wanted to study them. But I also wanted to do it in a completely different kind of environment, in Europe.

Actually, several people questioned whether it was a good idea to go to Europe, because there was this idea that if you went someplace outside the U.S., it would be harder to get a job or funding if you returned. But that's not the case. And for me it turned out to be a very good decision.

***You went to Eric Karsenti's laboratory, in Germany.***

Yes. One of my thesis committee members, Brian Burke, had done a post-doc at EMBL in Heidelberg. He knew Eric, and suggested I contact him. I read some of Eric's papers, and I thought, "Oh, this is

Text and Interview by Caitlin Sedwick
csedwick@gmail.com



HEALD AND MACMILLAN

**A perfectly symmetrical mitotic spindle organized around DNA-coated beads.**

it!" I interviewed with him, and it seemed like a really good fit, in terms of research topics. But it was a big transition for me; I had to learn to use an entirely new biological system, and I actually struggled a lot for the first couple of years. I just couldn't get an exciting result. I was really scrambling for a project and I started to worry.

The turning point came at a time when I was really depressed because nothing was working. I was wondering whether I was in the right laboratory, or what I should do to get things going properly. A kind post-doc in the laboratory offered to let me work with her on a subset of her projects. It would be something that I could work on, but it wasn't something that I had thought of myself, and I just didn't want to do it. I said, "Thank you, but no, I really have to continue beating my head against the wall until I actually figure out something of my own." That was when I realized I was actually serious about a career in science and that I was committed to making it work out.

## BREAKING FREE OF THE PACK

***And then you made a breakthrough…***

A few months later I was working with these chromatin-coated beads. I wanted to use them to figure out if phosphatases were recruited to mitotic chromatin. But I kept thinking to myself that the chromatin on my beads should generate microtubules, because Eric had micro-injected viral DNA into eggs and seen microtubules form around it. I wanted to see whether my chromatin-coated beads had this activity before I tried to purify the phosphatase, because purifying the phosphatase would necessitate using the swinging bucket centrifuge (I was actually terrified of these rotors) and chromatography—all stuff that I don't like nearly as much as microscopy. So I twiddled with the chromatin-coated beads, and then started to see, not only microtubules, but also bipolar spindles that self-organized around the beads. And suddenly I had this very accessible system with which to study this process. It wasn't that the concept was completely new, but it was a big breakthrough.

***It moved both the field and your career forward.***

Yeah, and as a result I got this great job at Berkeley. I actually interviewed in Europe as well, but at that point I thought that maybe the beads would be it for me. Maybe that would be the only thing that'd ever happen, the only major paper I'd ever have, so I'd better get a grant while the iron was hot. What if I stayed in Europe and floundered, and then ran out of money, and got stranded? But I think what I've realized since I started my laboratory—and, if I'd thought about it, might've realized as a post-doc—is that I do the best science when I interact with people from different areas of expertise. For example, the chromatin-bead experiment arose from my interactions with a laboratory down the hall.

**Heald savors the moment, having conquered a mountain.**

When you start your own laboratory, at first you think, "Oh, I have to just hunker down and figure everything out for myself." But I've realized that what I'm really good at is collaborating and identifying interdisciplinary projects. Most scientists are really open to combining forces and sharing the credit, and I think scientists shouldn't be afraid to work together more, to take risks and try out some far-fetched ideas.

***What ideas are you pursuing in your laboratory right now?***

The hot topic in my laboratory right now is intracellular scaling. We tend to work with egg extracts from *Xenopus laevis* for our mitosis studies. But recently I had a rotation student who made extracts from the eggs of *Xenopus tropicalis*, which is a smaller, related frog that lays smaller eggs. She made a really exciting observation—the extracts from *tropicalis* eggs generated smaller spindles even when we used the same chromosomes that we'd used in the *laevis* egg extracts. And if you mix extracts from both species', you get intermediate-sized spindles and nuclei.

**"Scientists shouldn't be afraid to work together more, to take risks and try out some far-fetched ideas."**

Some cytoplasmic activity determines how these structures intrinsically scale themselves, so we are thinking about whether this might explain how cellular structures and organelles shrink during development—when the egg divides into smaller and smaller cells. And now we have a system to study this. JCB

1. Heald, R., et al., 1990. *Cell.* 61: 579–589.
2. Heald, R., et al., 1996. *Nature.* 382: 420–425.
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4. Brown, K.S., et al., 2007. *J Cell Biol.* 176: 765–770.
5. Kalab, P., et al., 2008. *J Cell Sci.* 121: 1577–1586.