Rebecca Wright Heald

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Rebecca Heald is known for spindles, beads and bicycles. Heald's discovery while still a post-doctoral fellow that DNA-coated beads would stimulate *Xenopus* egg extract to self-mobilize a model spindle apparatus is only one spoke in a creative career that has fanned out in many directions. It has earned Heald, an associate professor of Molecular and Cell Biology at the University of California, Berkeley, the ASCB's 2005 Women in Cell Biology Junior Career Award.

"I think Rebecca is one of the most original cell biologists of her generation," says Tony Hyman, now at the Max Planck Institute in Dresden. "When she came to Eric Karsenti's laboratory [at EMBL in Heidelberg], the field of spindle assembly was at low ebb. The experiment that she designed using artificial beads to mimic chromatin revolutionized the field."

According to UCSF/HHMI investigator Ron Vale, Heald's contributions began as a graduate student with Frank McKeon at Harvard Medical School, during which time she provided key evidence that mitotic phosphorylation leads to disassembly of lamins and the breakdown of the nuclear envelope. Her DNA-bead discovery at EMBL, says Vale, became "one of the most interesting papers in the mitosis field of the past decade. It simplified the problem of spindle assembly (at least for meiotic spindles) both conceptually and experimentally."

More recent work with Karsten Weis demonstrating a Ran-GTP gradient substantiated a key premise of how microtubule assembly around chromatin works, says Vale. "In a completely different type of project, Rebecca's lab has developed a novel method for purifying spindle midbodies and identifying their components. This was a very ambitious study that went well beyond the proteomic analysis (most people would have stopped here!) and provided a complete functional analysis of the proteins identified."

"Rebecca has engaged in a dazzling number of extremely successful collaborations," says Barbara Meyer, an HHMI Investigator at Berkeley. Meyer says Heald has a knack for finding the most productive way to reach novel conclusions about chromosome architecture and spindle assembly, including the roles of motor proteins in chromatin-induced spindle assembly, chromatin-associated regulators, and the physical existence of the Ran-GTP gradient surrounding chromatin. "In each of these topics, the conclusions have been unexpected and ground breaking," says Meyer.

Heald pays attention to connections that others miss, says Indiana University's Claire Walczak, who won the 2004 ASCB WICB Junior Career Award. Heald's DNA-bead discovery is a prime example, says Walczak, a close friend and onetime collaborator. "It was one of those fortuitous accidents but it would have passed by a lot of people. The accident was stumbling across the spindle part, but Rebecca's insight was in immediately seeing what this meant and then figuring out exactly how it worked."

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It was an "accident" two fruitless years in the making, Heald recalls. After finishing her Harvard PhD in 1993, Heald chose the Karsenti lab in order to experience life in another country and work in another field. "But once I got to EMBL, I worked for two years on a variety of projects and had absolutely no success. This was a shock because when you have your PhD, you think you know a lot, but then you start out in a new lab and you know absolutely nothing. I'd switched topics and I'd also switched experimental systems."

The DNA-coated beads were an established lab technique to immobilize DNA on a substrate. Heald first saw them in Peter Becker's lab down the hall at EMBL in a *Drosophila* system to study chromatin assembly and dynamics. "No one had really used them for cell biology before," Heald remembers. "My idea was to take their system and use it with *Xenopus* extract for a biochemical assay of a mitotic kinase that I was interested in." Heald prepared the *Xenopus* assay and then put it under the

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confocal. "I saw a spindle had formed around some of these beads. I just couldn't believe it. We knew that chromatin has this kind of activity physiologically, but there had never been an easy assay to look at it before." In the egg extract, the beads were stimulating microtubule polymerization and the motors in the extract were organizing the microtubules into a spindle. After a few months of refining the assay, Heald remembers the day she looked through the confocal and saw "a perfectly symmetrical spindle that had formed around a line of beads that just happened to be in a row. You don't have any control over how the beads line up, but somehow they were placed exactly right. The picture finally silenced the last skeptics about whether or not these were really spindles."

Rebecca Heald was born in 1963 near State College, Pennsylvania, where her father was finishing a post-doc in Chemistry at Penn State; She grew up in Greenville, PA, after her parents joined the faculty of Thiel College. That's where Heald was first imprinted to chemistry. "I loved the smell of all the organic solvents in my father's building. Whenever I go into a chem lab, I always feel right at home," she says.

Yet Heald felt she had no special talent for chemistry and as an undergraduate at Hamilton College was torn between literature and biology. She says she made the "practical" choice to become a biologist on the grounds that she was a terrible writer. Ironically, Heald says that she spends most of her working life as a cell biologist reading and writing. Much of the prose flowing across her desk these days comes from her role as a monitoring editor for *The Journal of Cell Biology* and as a member of the NIH study section on Nuclear Dynamics and Transport.

At Berkeley, the Heald lab is in a semi-formal alliance with the labs of Karsten Weis and Matt Welch. The "Tri-Lab" shares equipment, ideas, advice and occasionally personnel, explains Welch. Besides the practical benefits, Welch says that it has been a great opportunity to watch a creative scientist like Heald up close. "Rebecca is not afraid to try new things," he says. "She's already done work in chemical biology, in proteomics and in other areas. A lot of people stick to the same old thing, but Rebecca is unafraid to venture into new territory." That's why she's such an effective mentor, Welch says. "Rebecca is a very flexible scientist herself so she lets people in the lab explore their own ideas. She isn't one of those micro-manager PIs. And the people who've come out of her lab have already done remarkably well."

Outside the lab, Heald is most likely indulging her other identity, as a bicyclist. "Cycling has always been Rebecca's outlet for keeping her sanity," says Claire Walczak. Fittingly, Heald met the man who was to become her husband, Steven Hill, on a ride through the Dolomites in Italy. Hill, an amateur cycle racer and professional computer programmer, and Heald were married in 2004 in San Francisco City Hall. "It was like going to the DMV except it was fun," says Heald. "You take a number and wait until they call you in. I totally recommend it."

Heald and Hill have put in considerable mileage on long distance bike trips through the French Pyrenees and the Pacific Northwest and on local runs through Berkeley where they live in a small rented apartment with an 8-year-old golden retriever named Eddie. "We have a car," says Heald, "but we put way more miles on the bikes. I don't own a house, but I own a titanium bicycle. It's a lot more affordable than a house in the Bay Area." ■

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