

Janet Shaw



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Janet Shaw drives to work each morning past the historic “This is the Place” monument at the mouth of Emigration Canyon where the founding Mormon fathers first beheld the Great Salt Lake basin. What may be less well known about Utah, says Shaw, is that it’s also a place that strongly supports biomedical research.

Professor of Biochemistry at the University of Utah and Leader of the Cell Response and Regulation Program at the Huntsman Cancer Institute, Shaw investigates mitochondrial membrane division and fusion in yeast and mammals. “It turns out that mutations in two of the [mitochondrial] molecules that play a role in [yeast] fusion have been linked to inherited neurological diseases in humans,” says Shaw. “Mutations in one cause dominant optic atrophy, a disease in which fibers of the optic nerve degenerate. Mutations in the other fusion gene are associated with Type 2 Charcot-Marie-Tooth Syndrome. This results in muscle weakness in the hands and feet, loss of sensation and foot deformities. These symptoms makes sense, because when you compromise mitochondrial function, you see the defects in tissues which require a lot of mitochondrial support—neurons and muscle.”

Utah provides a unique resource to explore those links, says Shaw, because of the Mormon genealogical tradition and because of the University’s independent Utah Population Data Base, which provides highly detailed family information. “We’re working with human geneticists here at the medical school to study how some of the mutations they’ve discovered in families affect mitochondria. We can look at mitochondrial behavior and function in tissues from patients and also see how these same mutations behave in the yeast system,” explains Shaw.

Shaw first learned yeast biology as a post-doc

in Bill Wickner’s UCLA lab. Wickner recalls that when Shaw first joined the lab, he put her on a difficult *in vitro* assay development project. She was making steady progress, Wickner recalls, but after a year he felt that her “post-doc clock was ticking” and that she needed a project of her own to take onto the job market. Shaw parked the assay project and set out to find a novel set of vacuole mutations, says Wickner. In the meantime, Barbara Conrad, a “fearless” new graduate student, arrived and volunteered to take on Shaw’s old assay. Wickner was astonished by Shaw’s ‘I’ll do anything to make this work for you’ reaction to Conrad. They worked as one. A year

later, they had the assay. “I think that shows Janet’s rigor and her selflessness. It’s what’s made her a great mentor and a great scientist,” says Wickner.

Another colleague and friend from Shaw’s post-doc days is Greg Payne, who was then a newly-hired assistant professor at UCLA. “We soon found out that we had a very easy time talking science,” Payne recalls. “Janet is very good at listening to someone’s science and thinking about it. It’s not a talent that you find in a lot of scientists who can talk about their work but have nothing to offer in return. Janet was a post-doc then and I was an assistant professor but I immediately felt like I was talking with a peer.”

When Shaw left for Utah and her own assistant professorship, their science talk continued. When Shaw called to explain why she was shifting

from vacuole inheritance to mitochondrial membrane behavior, Payne understood her experimental reasoning but recalls, “As a friend, I was a little worried. She was a new assistant professor and here she was changing the whole direction of her lab. I thought that took a lot of guts. Of course today, she is viewed along with people like Mike Yaffe as one of the founding

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members of what's become the next big line in yeast investigation."

Janet Shaw was born and raised in Tucson, Arizona, where her father owned three men's clothing stores; she worked part-time there from junior high until college. She summarizes that experience thus: "On the one hand, I learned that I didn't want to work in retail. On the other, I can still measure an inseam." Her mother taught community health nursing at the University of Arizona and often helped out with community genetic screening efforts. "When I was 13, my mom got me involved in a Tay-Sachs screening project, and that was a huge influence on my life," Shaw remembers. "In the seventh grade, I was telling people that I wanted to get a PhD in Genetics, even though I didn't have the faintest idea what that meant."

Luckily, she found out. Shaw started with a BA in Genetics from the University of California, Berkeley in 1982, and then a PhD in Molecular Biology from UCLA in 1990. Her mentor, Larry Simpson, studied mitochondrial DNA in *Trypanosomes* and other parasites. This was at the dawn of RNA editing, and Shaw recalls that, "nobody knew then that you could remove or insert individual nucleotides after RNA transcription. But *Trypanosomes* have this unusual way of controlling their mitochondrial gene expression by adding or deleting nucleotides after RNA transcription. We were seeing mitochondrial coding regions in which 50 percent of the nucleotides had been modified this way."

The exotic life cycle of *Trypanosomes*, however, made them poor basic experimental models, so Shaw moved to the Wickner lab to learn yeast genetics and apply them to vacuole formation. She didn't return to the mitochondrial field until she started her own lab at the University of Utah in 1993. Aside from the Yaffe lab, no one was using genetic approaches to study mitochondrial membrane behavior in eukaryotes, she reflects. Shaw started from scratch, screening for her own mitochondrial shape and movement mutants and moving on to clone genes and characterize their proteins. Now that basic work is paying off with new insights into mitochondrial regulation of apoptosis and the emerging link to human mitochondrial myopathies.

Shaw and her husband, Gary Drews, a plant biologist at the University, live in the upper reaches of Emigration Canyon. Life in the canyon is cooler in the summer and snowier in the winter compared to the city, says Shaw. In the snowy season, Utah's deep-powder ski country is in their backyard. They have an 11-

year-old Siberian husky, Laika, named after the first Russian dog in space.

The Utah angle has proved valuable in Shaw's recent work as a member of the ASCB Council. For the last three years, Shaw has made the rounds each spring on Capitol Hill with other Council members to brief members of Congress on biomedical research issues. "I'd never seen how Washington worked up close before," says Shaw, "but coming from a relatively conservative state, it gives me a little more credibility with certain people, although I always like to point out that Senator [Orrin] Hatch has been very supportive of stem cell research. In Utah, university researchers have always had a good relationship with our delegation, and their staffs have come to rely on us for solid information on these issues."

Shaw's Council term ends in December, but her Congressional education days may not be over: "I really enjoyed doing 'Hill Days' so now I'm thinking that I may come back on my own." ■

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