ASCB PROFILE

Barbara Hamkalo

The Hamkalo lab is closing this month. After 31 years at UC Irvine, Barbara Hamkalo will officially "retire" from the Department of Molecular Biology and Biochemistry at the end of June. But given the multi-tasking nature of modern academic life, Hamkalo will continue at Irvine for months to come in her halftime role as the Associate Executive Vice Chancellor for Space and Enrollment Management. "The important word here is 'Space'," says Hamkalo. "Space is more critical than money, especially at a university and, at Irvine, I'm the Czarina of space."

Barbara Hamkalo and Mei Ling

The University of California system's capital budget is supported by a bond program which has protected it from the state's budget implosion; construction at UC Irvine is going full blast. Hamkalo is planning one more major laboratory building along with supervising three other science and engineering projects in progress before she allows herself to fully retire.

> "Space is more critical than money, especially at a university and, at Irvine, I'm the Czarina of space."

> "Barbara's a wonderful organizer, but more importantly, she is highly motivated about the science, a good listener, and genuinely interested in other people's work. And she always has time for students."

The shutdown of the Hamkalo lab will leave a void in the chromatin and chromosome structure community. Joel Gottesfeld, who is at the Scripps Research Institute, has known Hamkalo and her work for thirty years. "Scientifically, Barbara has done a lot of excellent work on a very broad range of things", he says. "She pioneered *in situ* hybridization of specific DNA probes to localize where genes reside on chromosomes at the EM level. Likewise, she's used immunological probes to look at the distribution of proteins on chromosomes. She's also done a lot of ultrastructure work on chromatin, and throughout her career microscopy has remained a main focus."

> "Her leadership at UC Irvine has been so successful because of her commitment to making choices and decisions based on what was good for the institution and not on what would feed Barbara Hamkalo's ego."

Beyond her own lab, Gottesfeld says that Hamkalo helped what was a small special interest area become an accepted field and a dynamic scientific community. "Barbara and I were the co-founders of the West Coast Chromatin and Chromosome Meeting that's still held every December at Asilomar. For the first twenty years, Barbara was the driving force behind that meeting. She just knew everyone [in the field] and she was able to get them all together in one room—students, post-docs and faculty—and let everyone speak. Barbara's a wonderful organizer, but more importantly, she is highly motivated about the science, a good listener, and genuinely interested in other people's work. And she always has time for students."

During her tenure as Dean of the School of Biological Sciences at Irvine, Ellie Ehrenfeld, the former Director of the NIH Center for Scientific Review, talked Hamkalo into taking various temporary deanships, committee assignments and review panel posts. Ehrenfeld says, "Barbara's considerable scientific talents are separate from the strong administrative skills that I saw while working with her over the years at UC Irvine. Her leadership at UC Irvine has been so successful because of her commitment to making choices and decisions based on what was good for the institution and not on what would feed Barbara Hamkalo's ego. Barbara is somebody who likes to do things. People who take positions because they want to 'be somebody' often don't get things done. Barbara gets things done."

Born and raised in New York City, Hamkalo was the first and, as far as she knows, the only member of her extended family to pursue a scientific career. Her father was a postal employee,

her mother a homemaker. Her older brother is a professional musician. "Both my parents lost their fathers before they could finish high school and had to go to work to support their families," says Hamkalo. "So I'm exceptionally grateful to them for appreciating how important my long education was for me. My parents encouraged me every bit of the way, even if they could have had no idea of what grad school was about."

> "I was interested in science and there wasn't this demand in an all-girls school that you be a little stupid so the guys would like you."

Hamkalo is also grateful for her secondary education, at what was then an all-girls public high school, Washington Irving, in Lower Manhattan. "I was interested in science and there wasn't this demand in an all-girls school that you be a little stupid so the guys would like you," she recalls. But she got it out of her system and did not choose an all-girls' college. I thought, 'I've done that'," she says. Instead, Hamkalo went to co-ed Queens College in the days before it became part of the City University system. Her biology professors there were first class, she says, as were her grades. But Queens College had no research labs on campus; her professors did bench work elsewhere in New York. So when Hamkalo turned up as a graduate student in Paul Swenson's lab at the University of Massachusetts in Amherst, it was the first time she'd ever worked in a research environment. She took to it at once, embracing its frustrations as well as the occasional flash of insight.

> "Barbara was one of the many good young women who were beginning to appear in positions in science. Before then, there were good women in science but there were not so many of them. Barbara was part of that generation that established women in science."

Hamkalo worked with Swenson on physiological differences in *E. coli* that allowed them to repair UV-induced damage. Her actual thesis experiments had to be done in Tennessee after Swenson moved to the Oak Ridge National Laboratory. Rural Tennessee was an eye-opener for a New York City girl, says Hamkalo, and, after obtaining her UMass PhD in 1968, Hamkalo headed back East for her first post-doc in the newly established Harvard Medical School lab of Charles Thomas, Jr.

The late sixties was a heady time in Boston, both culturally and scientifically. As the DNA revolution built momentum, the structure of chromosomes became a pressing issue; how did they organize yards of linear DNA into a practical, storable, and unpackable genome? Thomas had done some of the first work probing genomic structure with phage at Johns Hopkins. He focused his lab at Harvard on unraveling the genomic structure of eukaryotic DNA which he hoped would lead to the Holy Grail of the eukaryotic chromosome. Hamkalo's EM background working with *E. coli* suited this ambition perfectly.

> Born and raised in New York City, Hamkalo was the first and, as far as she knows, the only member of her extended family to pursue a scientific career.

It was at the ASCB meeting in Boston in 1968 where Hamkalo bumped into Oscar Miller, an electromicroscopist she knew from Oak Ridge who'd startled the meeting with the first EM images of gene transcription in amphibian oocytes. Hamkalo wondered if Miller's technique could visualize *E. coli* gene transcription. When Miller came back to Boston to teach a summer course at Harvard, Miller and Hamkalo ran a three-week trial experiment. It was an interesting failure, but Miller offered Hamkalo a post-doc position to continue the work back at Oak Ridge. "Oscar said he would teach me everything he knew that I didn't and I

Micropipette Pullers
World-class quality!

Powerful: The laser-based **P-2000** puller remains the industry standard device for pulling fused silica, nanospray tips and optical probes.

Consistent: The **P-97** "workhorse" reliably fabricates a variety of tips: patch clamp, intracellular, transgenic and microinjection.

Economical: The simple and inexpensive **P-30** vertical puller suitable for basic and patch-type pipettes.

SUTTER INSTRUMENT
PHONE: 415.883.0128 | FAX: 415.883.0572
EMAIL: INFO@SUTTER.COM | WWW.SUTTER.COM

would do the same for him," says Hamkalo with a laugh, "but the only thing I knew that Oscar didn't was how to grow *E. coli*." In 1971, Hamkalo moved back to Tennessee and began a two-year slog to finally capture through EM some of the first images of prokaryotic transcription and translational regulation.

Hamkalo's lab probed into the histone structure of the centromere, particularly the "linking" H1 histone that appeared in a bewildering number of subtypes, fluctuating through the cell cycle yet offering no easy cloning target.

"I've always been a fan of hers," says Miller from Charlottesville, Virginia, where he is the emeritus Chairman of Biology at UVA. "At the time she came into my lab, Barbara was one of the many good young women who were beginning to appear in positions in science. Before then, there were good women in science but there were not so many of them. Barbara was part of that generation that established women in science as every bit as good as men. And she was one of the smartest. She knew a lot about some things and a little bit about a lot of things."

Miller recalls that when he took the chairmanship at UVA in 1973, he offered Hamkalo a faculty position but she turned him down, preferring to strike out in new directions at fledgling Irvine. New gene expression technologies and the new nucleosome concept were rapidly changing the terms of the chromosome debate. In setting up her own lab at Irvine, Hamkalo found herself drawn to the one area of the eukaryotic genome that seemed almost genetically inert, the centromere, where repetitious, non-coding heterochromatin was densely packed. Hamkalo's lab probed into the histone structure of the centromere, particularly the "linking" H1 histone that appeared in a bewildering number of subtypes, fluctuating through the cell cycle yet offering no easy cloning target. To identify and measure the various H1 subtypes, Hamkalo eventually came up with antibodies for all five varieties and with them an accurate method of predicting whether a gene would be activated, based on the disappearance of two of the main subtypes. "Basically we had a predictor of chromatin activity and we distributed those antibodies to lots of labs to do with as they pleased," says Hamkalo. "These reagents aren't much good unless they're available."

"She knew a lot about some things and a little bit about a lot of things."

Despite her successes, Hamkalo admits quite cheerfully that even after thirty years, the exact mechanisms of centromeric heterochromatin are still unknown. "It's still largely a black box because it's so unclone-able and the tandemly repetitive DNA is so discouraging to most researchers." Perhaps it was the sheer difficulty and the complexity of the subject that drew Hamkalo to the field. "I've always been attracted to problems that are closer to insoluble than soluble. Maybe I won't be able to get all the answers, but I might make some contributions that would get other people interested so they could pursue it."

Nancy Hutchison, recent winner of the ASCB-Bruce Alberts Award for Science Education, is a former Hamkalo graduate student, now at the Fred Hutchinson Cancer Center in Seattle. Her mentor taught her more than bench science, says Hutchison. "Barbara gave us lots of freedom in the lab. She was not one of those advisors who are always breathing down your neck and asking, 'Where are the results?' She was also a terrific connector, really comfortable about going to national and international meetings and coming back with new ideas and new names." One of these connections saved Hutchison's thesis experiment from becoming a technical nightmare when Hamkalo remembered a talk by Dave Ward that mentioned a new non-radioactive small molecule label for nucleotides. A call to Yale by Hamkalo produced an experiment-saving labeling molecule and a prestigious collaborator. "Barbara was able to make the connections I needed and she did that for everybody in the lab," says Hutchison.

Outside the lab, Hamkalo is known for her hospitality, including her great cooking, which centers at her house in Laguna Beach where she lives with her prized Lhasa apso, Mei Ling. She looks forward to wrapping up her administrative responsibilities at Irvine and spending more time at her house in Laguna. Hamkalo plans to travel more, cook more, and teach a little, particularly in an American Association of University Women tutoring program for girls interested in science, and at a UCI-affiliated program for retirees. ■