Mina Bissell

Cell biologist Mina Bissell left Iran at age eighteen and embarked on a career in American science. Her fearless approach and unconventional thinking have helped shape ideas about how breast tumors develop.

Few things scare Mina Bissell. She was fearless about leaving her home in Iran to attend college in the United States. She was undaunted by being one of only three women in a class of 200 to enter Harvard graduate school. And when her radical ideas about cancer biology stirred up opposition, she took it all in her stride.

Bissell, who is now a top-level scientist at Lawrence Berkeley National Laboratory in California, struggled to be taken seriously when she proposed that the tissue surrounding a cancer cell is just as important in shaping its behavior as the genes inside it. Today, that idea is not only widely accepted, but one of the hottest topics in cancer research. "It took a quarter century for people to recognize the importance of the [environment]," says cancer pioneer Robert Weinberg at the Massachusetts Institute of Technology in Cambridge. "Mina has always been a leader in this field".

At least part of Bissell's self-confidence can be traced back to her upbringing in the Middle East. Growing up in a family of academics, she engaged in political debates with her father and, like many other women in Iran, was encouraged to pursue a higher education.

When she ranked among the top of the country's high school students, the budding intellectual won a scholarship to attend an American college. "My father didn't want me to go—he felt that girls didn't get a proper education in the US," Bissell says. But she went anyway, and after abandoning English literature for science, earned both an undergraduate degree in chemistry and a Ph.D. in microbiology from Harvard University.

Bissell says she has always done "crazy stuff, even in grad school." Her doctoral thesis proposed the unconventional idea that enzymes fold into their final form only after they are secreted by the cell—a model that has since been proven correct. And when she became pregnant during her first year of graduate school she defied widespread expectations that she would drop out. "It just didn't occur to me that one quits," she says.

It was after Bissell joined the Lawrence Berkeley National Laboratory that she began her groundbreaking work on cancer. Toward the late 1970s, cancer was thought to arise when one or two genes in a cell acquire mutations and trigger uncontrollable proliferation. The meshwork of proteins and other molecules around it, known as the extracellular matrix, were thought to be a passive scaffold for these cells.

Bissell questioned that idea. She first showed that a particular virus was better at transforming normal cells into cancerous ones when the cells were growing in culture than when they were growing in embryos. This suggested to her that something about the surrounding tissue could control tumor formation.

When a research fellow in the lab began studying mammary gland development, Bissell began applying these same principles to breast cancer. She examined whether the three-dimensional structure of breast tissue, which alters dramatically during puberty, pregnancy and lactation, might influence cancer growth. Rather than studying breast cancer cells grown on two-dimensional culture plates, as was common at the time, she examined the behavior of cancer cells within clumps of tissue.

These experiments convinced Bissell that the extracellular matrix sends important signals to breast cells that alter their gene activity, and led her to propose a new model of breast tumorigenesis. She suggested that a normal cell converts to a cancer cell through a mutistep process, involving both genetic changes within the cell and signals from the extracellular matrix.

The idea met with stiff resistance from many in the cancer community, who were just beginning to use molecular genetics to identify cancer-causing oncogenes. "Everyone was focused on oncogenes," says long-time collaborator and cancer researcher Zena Werb at the University of California, San Francisco. "The fact that there might be outside controlling factors didn't sit well with many people".

A quarter century on, that view has changed. Thanks to studies in Bissell's lab and others, the extracellular matrix is now widely recognized as an important source of signals that regulate the changes in gene expression, cell division, survival, shape and movement that control tumor progression. Indeed, many of the scientists who initially questioned Bissell's theories are now themselves studying the environment in which tumors grow. And in the 2005 financial year, the US National Cancer Institute prioritized studies on the interaction between cancer cells and their surroundings.

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Bissell's passion for understanding cancer still dominates her lab. "The only law in the lab is that everyone has to work on the breast," says postdoctoral researcher Derek Radisky.

Her long-term goal is to develop a more realistic three-dimensional model of breast cancer that mimics its normal situation, and can be used to study cancer pathogenesis and test anticancer drugs. With this in mind, her 35-strong lab boasts a diverse array of bioengineers, cell biologists, physicists and stem cell biologists. Many pharmaceutical companies and researchers still screen potential drugs on two-dimensional tissue.

Despite her success, Bissell herself continues to challenge convention, as well as her colleagues. Coworkers and friends say that she sits and listens to radical ideas, rather than dismissing them out of hand—and always seems to side with the rebels. "She likes to be outside the mainstream," says Radisky. "She's not afraid to tell big shots that they're wrong."

But while Bissell will support those with up-and-coming ideas, she demands a lot in return. Lab members say she expects everyone to work with the same feisty fervor that she has long possessed. "I value someone who washes glassware really terrifically over a postdoc who isn't passionate about their research. You just have to find things that you love and do them well," she says.

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