Berkeley Lab life scientist **Mina Bissell** has become a giant among cancer scientists by pioneering a whole new field of research that she hopes will pave the way for a fresh class of treatment for all cancers. Bissell's breast cancer research holds real hope for taming cancer by changing it from a death sentence to a manageable, chronic disease. “You are not going to eradicate cancer,” said Bissell. “But you could keep it in check.” Bissell's ideas have gotten her worldwide attention and won millions in research grants.

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Cancer pioneer

Oncology community optimistic about scientist's discoveries

By Betsy Mason

Bissell

BERKELEY—Mina Bissell has become a giant among cancer scientists by pioneering a whole new field of research that she hopes will pave the way for a fresh class of treatment for all cancers.

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“You are not going to eradicate cancer,” said Bissell. “But you could keep it in check.”

Bissell's ideas have now gotten her worldwide attention and won millions in research grants, but they were not immediately embraced by the bulk of the cancer research community.

“They thought I was nuts,” said the Lawrence Berkeley Lab chemist.

Most researchers had focused on tumor cells and the genes that caused them to veer off the path of normal cell growth. These “oncogenes” undoubtedly play a critical role in cancer development, but not all cells with the genes become cancerous. And not all cancerous cells carry oncogenes.

It took an outsider with a background in chemistry and bacterial genetics, rather than cancer biology, to discover that the environment outside the cells in the breast play a critical role in determining whether those cells will grow into breast cancer.

“I think part of the reason I did this is because I didn't know any better,” said Bissell.

The network of proteins around breast cells, known as the extracellular matrix, was thought to be an inert scaffolding without a role in cell function. But this line of thinking never made sense to Bissell, who is part of a long tradition of trailblazing cancer research at Lawrence Berkeley Laboratory.

“I began to think that what actually holds this structure together may in fact tell the cells what they have to do,” she said.

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More than two decades later, the diminutive Iranian-born scientist can barely stay seated out of excitement while recounting the discovery. That energy undoubtedly helped her persevere when her ideas were shunned by the cancer biology community.

But now many cancer biologists share her enthusiasm and agree that understanding the role of the extracellular matrix could be key to finding effective treatments for cancer.

“It is very widely accepted,” said Berkeley lab geneticist Joe Gray, who also heads up the breast oncology program at UC San Francisco. Gray was initially skeptical of Bissell's ideas, but today agrees that the cell's environment is a key player.

The National Institutes of Health has even started a special funding program to encourage researchers to work on the subject.

“All of a sudden, in the last two or three years it has become a really, really big field,” Bissell said. “Now everybody and their aunt is doing some of the stuff we were doing.”

Bissell is finally being widely recognized for her groundbreaking work. In 2002, she received a $3 million, four-year Innovator Award from the Department of Defense's breast cancer research program. She has been honored by organizations around the world, including the Susan B. Komen Breast Cancer Foundation and the Discovery Health Channel. And in October, she was awarded a $2.5 million, five-year Department of Energy Distinguished Scientist Fellowship to continue her research.

This summer, at a breast cancer conference in Philadelphia, Bissell was treated like a rock star by the 2,000 researchers in attendance. Her talk, among the best attended, described how by changing the microenvironment around cancer cells in the lab, she was able to coax them into reverting back into normal cells.

In a run-of-the-mill petri dish where cells are studied in a single two-dimensional layer, breast cancer cells are indistinguishable from normal breast cells. They look identical and all behave as normal cells.

But when Bissell and a collaborator in Denmark put human breast cancer cells into a protein gel that mimics the extracellular matrix, like a sort of three-dimensional petri dish, they began to form tumors, while normal cells did not.

This finding gave scientists a much-needed test to tell cancerous cells apart from normal cells in just two days.

Bissell's most recent work has focused on how the cells actually receive information from the surrounding structure. She has found that by manipulating the signals sent to a cell by its environment, she can cause potentially cancerous cells to become malignant, and then push them to revert back into normal cells.

By exposing tumor cells to an antibody that blocks the cell's receptors that receive cues from the extracellular matrix, Bissell was able to drastically reduce the number of cells that actually become tumors.

This discovery has researchers salivating for the potential cancer-suppressing treatments it suggests are possible. “This definitely has therapeutic implications,” said Gray.

Bissell's work has ushered in a whole new era of hope for breast cancer patients, and very likely for people suffering from other cancers as well.

“I think what we have done for the breast is applicable to every other kind of tissue and every other type of cancer,” Bissell said.

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