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Bissell Interview with Silicon Valley Biz Ink 2003

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Past Berkeley Lab chief guns for breast cancer

Mina Bissell was promoted to distinguished scientist at Lawrence Berkeley National Laboratory last year and returned to full-time research there after 16 years directing the lab's life sciences division. Last year she also was elected a fellow of the American Academy of Arts and Sciences. The academy recognizes accomplished scientists, many of whom are Nobel and Pulitzer prize winners. In 2002, Bissell received an Innovator Award from the U.S. Department of Defense's Breast Cancer Research Program. The award came with a $3 million grant. Associate editor Lynn Graebner talked with Bissell about her research, once considered unorthodox, and her vision for how to treat this deadly disease.

How did you become interested in breast cancer research?

My background is actually in chemistry and bacterial genetics. I did postdoctoral work on virology and I looked at tumor viruses.

There's a famous guy, Peyton Rous, who won the Nobel prize for discovering the first cancer virus, called Rous sarcoma virus. [My associates and I] showed early in my independent career that if you inject this virus into a chicken, you would get a tumor as Rous had shown. If you inject it into the chick embryo, the virus integrates but doesn't form tumors. So that showed that even a very potent cancer gene in different contexts can do different things.

I felt we needed to study the importance of context and what we refer to as the microenvironment of the cell when we do experiments in the laboratory.

I wrote a theoretical paper in January 1982 in which I proposed that the extracellular matrix -- very large molecules outside the cell
-- actually could contain information, they could be telling the cells what to do. This signaling could lead to information in the nucleus
to make profound changes.

And that led to the $3 million grant from the DOD?

They wanted to give the money for innovation. Throughout my career, I had done things that were unorthodox and now proven to
be true. I used the concept that extracellular matrix is important and with my collaborators in Denmark, we developed a very rapid
three dimensional assay, (a test) to distinguish normal and malignant cells outside the animal.

How could this lead to treatments? Because we can distinguish normal and malignant cells from each other, we can treat these
cultures, because each of the structures found is like a mini breast or a tumor. One of the things we did a few years ago was to treat
human breast tumor cells in 3D with antibodies or signaling inhibitors, and we could revert the malignant phenotype. These treated
cells literally revert themselves and look normal, even though their genome is totally malignant.

You can make a malignant cell healthy?

I don't know that I can make it healthy, but I can stop it from acting like a malignant cell -- at least in the laboratory.

So your research, while perhaps not curing breast cancer, could help develop treatments that could allow people to live a
normal life for much longer?

Yes, and I think the assays we've developed can be used in two ways. We could see what drugs can kill the tumor cells and keep
the normal ones. The important thing is to change the quality of life and to be able to come up with therapeutic agents that are not so
toxic and that are able to delay and kill enough tumor cells and revert others so that the cancer can't progress. The second way is to
come up with individualized therapies for patients.

In general I don't talk about cancer eradication; I talk about stopping the spread of the cancer and also learning how to cure the
patient. But we have to remember that the cause of breast cancer and many other forms of cancer has a lot to do with aging and
with the fact that we abuse our bodies.

How do we deal with the effect of aging on cells?

We ought to have a healthy lifestyle. For example, obesity is one of the worst culprits for all kinds of cancer. Obesity allows
undesirable chemicals to build up in your body and those things are always giving the wrong signal. But we also know, for example,
that exercise is a wonderful positive thing. It not only helps you keep in shape, it also allows formation of pheromones and
counteracts prostaglandin's (fatty acids that act as hormones in the body).

Our work shows the supreme importance of microenvironment -- everything that is outside our cells including cells surrounding cells
that become cancerous. If you keep them healthy, even if there is a mutation, you delay the onset of cancer or hopefully prolong it
forever from becoming cancerous.

How will the assays you are developing help treat breast cancer?

We are trying to make small replicas of human breast (tissue) in culture. These could be used for testing individual drugs and
combinations of drugs.

The assays also tell us what the important molecules and pathways are that keep a breast healthy.

The most important molecules are the chemicals in your body-- your genetic makeup, what you eat, what you breathe, how much
alcohol you consume, how much you exercise, how overworked you are....

The healthy structure of the breast is what allows the breast to function and, if one can keep that structure intact, then it is my thesis
that cancer would not manifest itself no matter how many mutations you have or, in some cases, even if you have a genetic
predisposition [for breast cancer].

Can men get breast cancer?

One percent of people who get breast cancer are men. They get a very, very virulent form.

What is really important is basic research; unexpected findings in unexpected places are very important.

I did not go out trying to help breast cancer, I went out there to try and understand some fundamental basic problems. It's very

uplifting that these many different organizations have understood that they need to support work on the function of normal breasts as well. If you don't understand how a normal cell remains normal, you're never going to understand how it becomes cancerous.
Everything is interconnected.

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