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Tricking Cells, Scientists Tease Cancer

For 30 Years, Scientist Has Examined Genes to Determine Causes of Breast Cancer BY <u>Cheryl Pon</u> Contribution Writer Wednesday, November 16, 2005

courtesy/mina bissell Scientists at Mina Bissell's lab have found that breast tissue's structure and function are related such that the loss of structure in a tissue could lead to cancer.

This year, the disease that can affect your mother, grandmother, sister, girlfriend, or any friend will kill 40,410 women. It's a disease that every woman, and some men, is susceptible to and which also has the lowest population awareness.

According to the American Cancer Society, there are slightly over 2 million women living in the United States who have been treated for breast cancer. In this year alone, about 211,240 women in the United States will find that they have invasive breast cancer.

Researchers in the Life Sciences Division at Lawrence Berkeley National Laboratory are working to determine breast cancer's causes. They have discovered that the structure and function in a tissue are intimately related and that the loss of structure in a tissue could lead to cancer.

Mina Bissell, a Lawrence Berkeley National Laboratory scientist who researched environments of cells and genes in determining the formation of tumors and breast tissue formation and structure, has studied breast cancer for over 30 years.

"I began to question how breast cancer is tissue-specific, in that you and I come from a single cell that makes breast, elbow, all of those," Bissell said. "Cancer of the breast is not the same as skin or liver cancer so in order to understand cancer we have to absolutely understand what it means to (have normal cell tissues)."

The American Cancer Society cites the chances of a woman having invasive breast cancer some time during her life as about one in eight. Breast cancer ranks second among cancer deaths in women.

"I began to question if there would be a single mutation or gene that would cause the cancer and that mutations of breast would occur within every single cell of the body to the extent that having that mutation isn't sufficient enough to cause cancer," Bissell said.

Bissell sought to answer these questions by taking cells from a pregnant, lactating mouse and adding hormones to it in a dish.

"It completely changed and forgot it was a breast cell. (It) lost its shape and characteristics," Bissell said. "So there must be something else in the body that tells it is a breast."

Bissell's lab then made a 3-D model of a breast unit in a culture and showed that when a malignant cell was placed on it, the breast unit formed a tumor rather than getting organized.

"The breast lost the ability to recognize the structure of the tissue when malignant," Bissell said.

Bissell then examined the numbers of receptors on the cell member of both normal and malignant cells and found that the amount of receptors on the malignant cells were much higher than those of the normal. Receptors are useful in that they tell the genes how to organize their structures.

Bissell made the tumor cells "think they were normal by reducing the ratio, their genome was a mess but the structure of the tissue was normalized."

What Bissell found was that when the specific oncogen, or cancerous gene, RSVirus was injected into a chicken a tumor formed. When injected into a chicken embryo, however, no tumor formed.

"The same tumor that causes cancer in the breast doesn't in the gut. The context of the breast and the gut depends on whether these genes can become oncogens," Bissell said. "We can take a really frank malignant human breast cell and make it normal but they were still malignant on the inside."

Bissell found that the extracellular matrix, or large molecules such as collagen, that cells secrete had information that signal to these cells.

"We then took a mixture gelatinous of these molecules and called it an extracellular matrix gel and we put the breast cells on top of these and they formed into a small breast and secreted milk," Bissell said. "It was very exciting."

An enzyme MMP3 was then used to destroy extracellular cell matrix around the breast cell taken from a pregnant mouse. The researcher noticed that involution occurred, which is when mammals stop secreting milk.

"This was exciting because extracellular matrix was responsible for maintaining milk and when the animal began to age they formed mammary tumors so this was revolutionary because without introducing oncogen and by manipulating the microenvironment and the architecture of the breast we could make it malignant."

The best and only prevention of breast cancer is to get a mammogram, as the earlier breast cancer is detected, the more successful treatment can be. Though many people worry about the radiation given off by mammograms, the American Cancer Society says that "One mammogram gives off roughly the same amount of radiation a person would get flying from New York to California on a jet plane."

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