

Hints of virus reemerge in breast cancer

Surprising new evidence promises to revive a controversial claim that medical detectives dismissed as spurious many years ago. Cancerous breast cells often contain genetic sequences characteristic of an infectious virus that triggers mammary tumors in mice, reported virologist Beatriz G.-T. Pogo of Mount Sinai School of Medicine in New York City and her colleagues at a cancer meeting this week. In contrast, normal breast cells rarely possess these viral sequences, the group reported.

The new findings raise once again the provocative, decades-old question of whether an infectious virus plays a role in at least some breast cancer.

"It would be extremely exciting and interesting, if true," observes Harald zur Hausen of the German Cancer Research Center in Heidelberg.

Over the last few decades, investigators have linked a number of viruses, specifically retroviruses, to cancers in animals and people. A retrovirus can transform a normal cell into a cancer cell by inserting its genetic material into the genome of the cell and disrupting the functions of crucial genes. Mouse mammary tumor virus (MMTV), for example, produces cancer in about 95 percent of the mice it infects.

Hints that a virus might also cause some human breast cancer date back to the 1930s, when scientists identified viruslike particles in mothers' milk. Mice transmit MMTV to their offspring through milk, but epidemiological studies provide no evidence that children breast-fed by mothers with breast cancer face an increased risk of the disease.

Still, over the last few decades, various research groups have reported some evidence, genetic and otherwise, that an MMTV-like virus is associated with human breast cancer, notes Pogo. Most of those reports were suspect, she explains, because scientists could not distinguish at the time between MMTV-like viruses and human endogenous retrovirus (HER), an apparently ancient virus whose genetic code is integrated into everyone's genome.

In recent years, scientists have sequenced many of MMTV's genes and have discovered regions of various genes that differ significantly from those in HER. Pogo's group took advantage of that knowledge—and of a method called polymerase chain reaction (PCR)—to search samples of human breast tissue for MMTV-specific gene fragments.

Last fall, in the Nov. 15, 1995 *CANCER RESEARCH*, the group reported that in almost 40 percent of breast cancer tissue samples they tested, PCR detected sequences similar to those in MMTV's *env* gene. Fewer than 2 percent of normal breast samples tested positive for the MMTV *env* sequence, the researchers found. Like similar genes in other viruses, MMTV's *env* gene encodes a protein that helps form the outer surface of the virus.

In a presentation this week at the American Association for Cancer Research meeting in Washington, D.C., Pogo's group reported that PCR detected a different partial sequence of MMTV's *env* in 13 of 19 breast cancer samples and in none of the normal breast tissue samples.

Moreover, hormones such as estrogen stimulate the activity of an MMTV-like *env* gene in a cell line derived from breast cancer cells, they found.

Considering the history of this issue, Pogo is reluctant to conclude that an infectious virus causes some portion of breast cancer cases. She says her group may simply have found a novel endogenous retrovirus, though she notes that would not explain why its genetic sequences are detected only in cancer cells. The group is now trying to find the complete viral sequence inside breast cancer cells.

zur Hausen, while attempting to replicate Pogo's results, is one of many researchers skeptical that the claim will hold up. "I don't think too many people will believe this," adds Susan R. Ross, an MMTV researcher at the University of Pennsylvania School of Medicine in Philadelphia.

— J. Travis