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*

Mom-child relations withstand day care

Regular child care provided outside the home or by someone other than the mother does not in itself undermine healthy emotional connections between mothers and their 15-month-old infants, according to a long-term national study. The finding holds even if care begins during the first 3 months after birth and runs for 30 hours or more per week, investigators contend.

Among infants who receive insensitive, unresponsive care from their mothers, however, the mother-child relationship takes a hit from low-quality child care, 10 or more hours per week of child care, or several shifts from one nonmaternal arrangement to another.

"This study helps us tease apart complexities regarding child care that have not previously been assessed," contends Jay Belsky, a psychologist at Pennsylvania State University in University Park and one of 25 scientists at 14 universities nationwide involved in the ongoing project. "But the jury is still out on the long-term effects of child care on development."

Belsky and several of his colleagues announced their findings last week at the International Conference on Infant Studies in Providence, R.I.

The investigation consists of 1,153 children and their families living in or near Boston, Little Rock, Seattle, and seven other locales. The youngsters, no more than 1 month old when they entered the study in 1991, will be tracked until age 7 years.

Experimenters administered questionnaires to mothers in their homes and videotaped them interacting with their kids at ages 1, 6, and 15 months. Independent observers rated the quality of each mother's child care efforts and noted infant irritability and other "difficult" temperamental traits.

At 15 months, infants completed a procedure in the laboratory during which their mothers left them alone in a room for a few minutes. Researchers theorize that a "securely attached" infant calms down and reestablishes contact with its mother after a brief separation, while an "insecurely attached" infant either ignores and avoids her or shows no signs of reassurance upon her return.

Unlike most previous studies, this one allows researchers to control statistically for each mother's personality traits, her adeptness at child rearing, and other important family influences before evaluating child care's contribution to infant attachment, asserts study coauthor Sarah Friedman of the National Institute of Child Health and Human Development (NICHD) in Bethesda, Md. NICHD funds and coordinates the project.

After taking family factors into account, Friedman states, researchers found no relation between infants' attachment security and type of child care, quality of care, number of hours per week in care, number of child care arrangements experienced, or age of entry into care—with one exception. Infants with insensitive, unresponsive mothers more often showed insecure attachment when given poor quality or large quantities of child care, she holds.

Boys who spent more than 30 hours per week in child care exhibited slightly more insecure attachment than other boys. In contrast, girls who spent 10 or fewer hours per week in child care showed a modest rise in insecure attachment.

Boys may react more negatively to their mother's extended absence than girls, asserts Eleanor Maccoby, a psychologist at Stanford University. Yet evidence suggesting that girls benefit emotionally from maternal separation probably will not hold up in analyses of children at later ages, Maccoby argues.

Quality of child care may assume much more importance when researchers conduct future examinations of kids' social, language, and cognitive skills, she adds. —*B. Bower*