BRCA1's role in cancer that's not inherited

Two groups of scientists have further tarnished the reputation of a gene linked to some hereditary cancers. At least 10 percent of nonhereditary ovarian tumors, they suggest, may result from a flaw in the BRCA1 gene.

A third group has found evidence that BRCA1 plays a role in some nonfamilial breast cancers as well. The triad of reports appears in the April NATURE GENETICS.

BRCA1 first attained notoriety last fall, when researchers announced it was responsible for some cases of inherited breast and ovarian cancer (SN: 9/24/94, p.197). At that time, there was no evidence of this gene's involvement in sporadic breast and ovarian cancers — malignancies that strike women without a family history of such tumors.

"These [new] findings are the first to implicate BRCA1 directly in sporadic tumorigenesis," says Jeff Boyd of the University of Pennsylvania Medical Center in Philadelphia. Boyd wrote a commentary that appears in the same issue of the journal.

Taken together, the results suggest that this gene may be involved in a significant fraction of the 182,000 breast and 26,600 ovarian cancers that will strike women in the United States this year.

Scientists suspect that a properly functioning BRCA1 serves as a tumor suppressor gene, carrying the blueprint for production of a protein that curbs cell growth. With little or none of this protein, breast or ovarian cells may start to proliferate wildly.

In the first report, Sofia D. Merajver of the University of Michigan Medical School in Ann Arbor and her colleagues studied samples of 47 ovarian tumors. None came from women with a strong family history of such cancers.

In four of these cases, the team found mutations in BRCA1. Their results show that the tumors are sporadic in nature — that is, they arise from a single ovarian cell with a BRCA1 gene that sustains damage at some point in life.

"The prospect that whatever you do might actually be of help to millions of patients around the world is incredibly exciting," says Merajver.

A second paper, this one by immunogeneticist John Trowsdale of the Imperial Cancer Research Fund in London and his colleagues, adds to the ovarian cancer story. His team studied 17 women with ovarian cancer that could not be traced back through their family.

That probe turned up one BRCA1 mutation in an ovarian tumor. In contrast, blood cells taken from the same woman revealed no such genetic flaw, indicating a sporadic cancer. People with familial ovarian cancer have the same BRCA1 mistake in every cell of their body, Trowsdale notes.

As for breast cancer, researchers have yet to find a BRCA1 flaw in nonfamilial cases of the disease. Merajver's team has been looking. She hints that the search will not prove fruitless. Trowsdale and others think mutations in sporadic breast tumors will be the exception rather than the rule.

But BRCA1 may yet prove pivotal in some cases of nonfamilial breast cancer. A third team has evidence of a mechanism by which this gene may bring about such cancer.

Jeffrey T. Holt of Vanderbilt University School of Medicine in Nashville and his colleagues studied breast tumors obtained from women with no family history of this cancer. The team discovered that BRCA1 expression in these tumor cells lags far behind the gene's activity in normal breast cells.

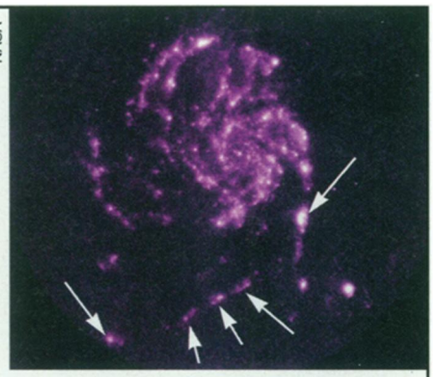
When Holt's team used so-called antisense molecules to inhibit BRCA1's function, they found that both normal and malignant mammary cells grew rapidly. The result implies that any lessening of the gene's activity in breast cells may lead to unchecked cell growth and ultimately to cancer.

BRCA1 researcher Mark H. Skolnick of the University of Utah in Salt Lake City calls the Vanderbilt team's results "very exciting." Skolnick led the team that first homed in on BRCA1, which is located on chromosome 17.

Skolnick, Holt, and other researchers think a flaw in an unidentified gene, one that regulates BRCA1 activity, could lead to sporadic breast tumors. If confirmed, such findings might someday lead to a treatment for some breast cancers that relies on boosting BRCA1 expression, Holt adds.

Such research remains the first step in elucidating BRCA1's role in breast and ovarian cancer. "We need to continue working to understand how this gene works," Merajver says, adding that the gene may be involved in other cancers too. "BRCA1 potentially has an enormous role to play in sporadic carcinogenesis." — *K. Fackelmann*

Galaxy M101: An ultraviolet portrait



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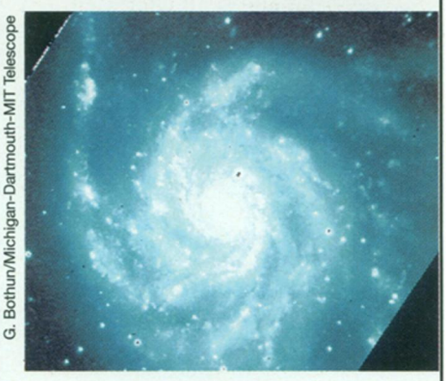

G. Bothun/Michigan-Dartmouth-MIT Telescope

Clusters of hot, young stars flaunt their brilliance in the first far-ultraviolet photograph ever taken of the spiral galaxy M101 (top).

NASA released the picture, taken March 9 by the Ultraviolet Imaging Telescope (UIT), late last week. The telescope, one of three ultraviolet instruments collectively known as Astro 2, flew aboard the space shuttle for 16 days last month. Observations in the far ultraviolet require the vantage point of space because Earth's atmosphere blocks most of the radiation at these short wavelengths from reaching the ground.

Several of the young, massive star clusters — marked by arrows — rival entire dwarf galaxies in size. The brightest cluster (lower left arrow) may have been forged in a collision between M101 and another galaxy.

The young stellar groupings stand out sharply in the far ultraviolet because they glow brightly at short wavelengths, whereas most older, cooler stars do not, notes UIT principal investigator Theodore P. Stecher of NASA's Goddard Space Flight Center in Greenbelt, Md.

In contrast, the galaxy's center appears fuzzier in the visible-light image of M101 taken from the ground (bottom) — even though this image is as sharp as the ultraviolet picture. This fuzziness stems from the large, diffuse mix of old and young stars that radiate in visible light.

Susan G. Neff of the Goddard Space Flight Center notes that in several of the UIT images, ultraviolet light emitted by galactic star clusters scatters off dust lurking behind them. By revealing the hidden dust, the images will aid astronomers in estimating the total amount of unseen, or dark, matter that galaxies harbor.

— R. Cowen