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Breast Cancer Drugs May Slow Growth of Lung Cancer

A few years ago researchers discovered that, much like breast tumors, some lung tumors also thrive on estrogen. Now a medical student conducting research on a Howard Hughes Medical Institute (HHMI) fellowship and colleagues have managed to stop the growth of human lung cancer cells in mice with a class of breast cancer drugs called aromatase inhibitors.

The studies are reported in the December 15, 2005 issue of the journal *Cancer Research*.

"It was a natural progression of the work that had already been done linking estrogen and lung cancer," said Olga Weinberg, who delayed her fourth year at Vanderbilt University School of Medicine to work on the project.

"Without aromatase, you don't get estrogen."

- Olga Weinberg

The findings suggest a new way to treat lung cancer in women - a group whose death rate from the disease is surging.

"More women are dying now from lung cancer than from breast cancer," said senior author Richard Pietras, Weinberg's research mentor at the University of California at Los Angeles. "We followed one of the clues as to why this is happening, namely that estrogen drives the growth of certain types of lung cancer in women."

To see if they could block this growth, the team started with the enzyme aromatase. It presented a natural target because aromatase converts testosterone into estradiol, a potent form of estrogen also used in hormone replacement therapy. In addition, drugs that inhibit aromatase have already made it to market as new treatments for breast cancer.

"The production of estrogen takes several steps, and aromatase is the key to the process," said Weinberg. "Without aromatase, you don't get estrogen."

To confirm that lung cancer needs aromatase, the team first searched for the enzyme in laboratory-grown lung cancer cells. After finding it there, they also searched 53 non-small cell lung tumor samples from patients. Using an antibody specific for aromatase and immunohistochemistry techniques, they found that 88 percent of the specimens from women and 86 percent from men contained high levels of the enzyme.

“Then we started getting excited,” said Weinberg. The team proceeded to highlight actual aromatase activity with a radioactive tracer, finding the enzyme active in both the laboratory cells and the frozen specimens. They double-checked by depleting the cells of estrogen, then feeding them testosterone: If aromatase was at work, the cells would produce estrogen. They did.

“Once we saw that aromatase was active, we wanted to see if we could inhibit it with the same drugs they use for breast cancer,” said Weinberg. The team treated their cells with the drug anastrozole for 48 hours, finding that it did in fact shut down aromatase activity and retard tumor growth in the lab.

“We found that tumors with both high and low levels of aromatase were sensitive to the drug,” said Pietras.

Finally, the team grafted human lung tumors onto mice. One group of mice received anastrozole for 21 days, while a second group did not. The tumors in the mice taking the drug grew 90 percent slower than the tumors in the untreated mice.

“It was such a natural progression that, although no one had looked at aromatase inhibitors in lung cancer before, it was just a matter of time before someone did,” said Weinberg, who hopes the publication will launch her planned career as a pathologist. “I always wanted to work with cancer, and I also wanted to learn about pathology. The HHMI fellowship let me do both for a year.”

HHMI awards medical student research fellowships to enable medical students to spend a year during their medical training doing research. The Institute wants to encourage medical students to think about careers in research.

As Weinberg finishes her medical degree at Vanderbilt University School of Medicine this year, Pietras and colleagues at UCLA have begun testing several other aromatase inhibitors against lung cancer. They hope to progress to human clinical trials, which should progress quickly since the drugs already have FDA approval.

Other contributors to this research at UCLA included Diana Marquez, Michael Fishbein, Lee Goodglick, Hermes Garban and Steven Dubinett. The National Cancer Institute Lung Cancer SPORE Program and the Stiles

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