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Genetic clue to cancer prognosis

Among women who have had breast cancer surgery, those with extra copies of a gene believed to be involved in the cancer process appear to have an increased chance of recurrence, according to a new study. Knowing who is likely to develop metastases would allow doctors to undertake preventive chemotherapy in only those people who need it.

According to the oncogene theory of cancer development, human cells carry certain genes that, when mutated by stimuli such as radiation or carcinogens, can trigger unbridled cell division. Researchers from the University of California at Los Angeles, the University of Texas at San Antonio and Genentech, Inc., in South San Francisco discovered one to 20 copies of such an oncogene, HER-2/*neu*, in cells from excised breast tumors. In previous studies, other researchers had found multiple copies of HER-2/*neu* in a breast cancer cell line growing in culture.

The breast cancer study needs to be expanded and confirmed before its results are applied routinely, the researchers say. In the meantime, the finding suggests the amplified gene may play a role in the initiation, establishment or spread of breast cancer, which strikes about one in 13 women in the United States.

At present, predicting the likelihood of recurrence in women treated for primary breast cancer is extremely difficult. The best indicator is the presence of cancer in the lymph nodes. But 25 to 30 percent of women who are negative by this measure will have a recurrence, says William L. McGuire of the University of Texas, one of the researchers.

Treating all node-negative women will result in many women being needlessly exposed to chemotherapy; not treating the group exposes certain members to life-threatening recurrences. Some physicians, says McGuire, treat all their patients; others make individual decisions based on other factors, including tumor size, stage of disease and presence of hormone receptors on the tumor cell surfaces.

In the study, reported in the Jan. 9 SCIENCE, gene amplification proved to be as accurate as lymph node involvement in predicting subsequent recurrence. Whether gene amplification will replace or supplement lymph node studies depends on confirmation of that work and further research, McGuire says.

The researchers initially found not only the oncogene but in many cases extra copies of it in 19 of 103 fresh tumor samples. They then tested cells from 86 breast cancers that had been stored an average of nearly four years; 34 showed amplification.

When they checked the relationship between amplification and cancer spread in this second group, they found a significant correlation with metastasis. In addition, the more copies of the gene, the worse the prognosis. After four years, for example, about 60 percent of women with no amplification were cancer-free, compared with about 35 percent of women with more than five copies of the gene.

Extra copies of other oncogenes are associated with recurrences of neuroblastoma, a rare childhood cancer (SN: 4/20/85, p.248), and of a particular type of lung cancer. Amplified genes are already being used to predict the outcome of neuroblastoma.

The presence of gene amplification in existing tumors suggests that it may be worthwhile to look for amplification in conditions thought to be premalignant, such as certain types of fibrocystic breast disease, says Dennis J. Slamon of UCLA, who headed the study. In addition, he says, determining whether there is a difference in the presence or degree of gene amplification in primary tumors and satellite growths could shed light on when amplification comes into play.

—J. Silberner