



### **Impervious.**

A mutation in the NQO1 enzyme makes breast cancer cells harder to treat and more likely to spread.

Credit: NCI

## **Mutation Spells Bad News for Breast Cancer Patients**

By Elsa Youngsteadt

ScienceNOW Daily News

30 May 2008

Breast cancer patients with a mutation in both copies of the *NQO1* gene have a 20% lower survival rate 5 years after treatment than do patients without the mutation, according to a new study of more than 2000 Finnish women. Those with the mutation were also four times less likely to respond to a common type of chemotherapy.

*NQO1* encodes an enzyme that protects cells from oxidative stress, damage to the cell and its DNA caused by reactive byproducts of metabolism. The NQO1 enzyme also helps to stabilize p53, sometimes called the "guardian angel" protein for its crucial role in preventing tumors. Because NQO1 protects a cell's DNA and its anticancer proteins, mutations that compromise the NQO1 enzyme are pernicious. One mutation, called NQO1\*2, increases the risk of cancer or cancer relapse, especially for leukemia.

A group of researchers at the University of Helsinki in Finland thought *NQO1* could also be a promising predictor of survival for women with breast cancer. The team followed the cases of 1005 women who visited the Helsinki University Hospital for breast cancer treatment between 1997 and 2004. They tested the women for the NQO1\*2 mutation and compared their survival rates over an average of nearly 6 years of follow-up visits. Only 65% of women who carried two faulty copies of the gene were alive 5 years

after treatment, compared with 85% and 87% survival for women with one and two good copies, the team reports today in *Nature Genetics*. The mutation also increased the chance that the cancer would spread. What's more, the mutation seemed to make the breast tumors resistant to a common form of chemotherapy, epirubicin. Women with two copies of the *NQO1*\*2 mutation had only a 17% survival rate 5 years after the therapy, compared with a 75% survival rate for women with at least one good copy of the gene. For radiation or hormone therapy, the *NQO1*\*2 mutation seemed to make no difference.

To confirm their results, the researchers studied a second group of 1162 women treated at two other Finnish hospitals. Again, they found reduced survival: Over 10 years, 46% of women with two copies of *NQO1*\*2 survived, compared with 75% of women with at least one normal *NQO1* gene. As in the previous group, the effect was most pronounced among patients who received chemotherapy rather than radiation--but most women in the second group had received an older kind of chemotherapy, so the researchers couldn't confirm the effect of the *NQO1*\*2 mutation on the now-common epirubicin therapy.

Nevertheless, "the results are pretty dramatic," says Carl Blomqvist, a cancer clinician and an author of the study. "The immediate thing to be done," he adds, is to launch a new clinical trial designed not just to detect the association between *NQO1*\* and prognosis, but to really test the predictive power of *NQO1*\*2 on cancer prognosis in women randomly assigned to epirubicin and other therapies. If the connection holds, it could give doctors another piece of information to help them choose the right treatment for a patient.

"It's an important finding," says David Ross, a toxicologist at the University of Colorado, Denver. He, too, emphasizes the need for a new clinical trial to confirm the connection between *NQO1*\*2 and prognosis, and he adds that the cause of the effect remains unclear. "There still need to be some t's crossed and i's dotted," he says.