

## 2 proteins may be survival markers in some breast cancers

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New research suggests that the presence or absence of two proteins may be important markers for long-term survival in some breast-cancer patients.

One of the proteins, called ErbB-4, is important for the growth and differentiation of several types of cells in the body. The second protein, called Wwox, is a tumor suppressor – it helps prevent cells from becoming cancerous – and it is missing in many breast cancers. Scientists don't yet understand how it works.

The research shows that the two proteins work together, and that their absence is associated with shorter survival in breast cancer. Furthermore, the study shows that Wwox keeps ErbB4 on the cell surface, and that this is associated with better survival.

The study was done by researchers at the Ohio State University Comprehensive Cancer Center in collaboration with researchers in Finland, and it was published in a recent issue of the journal *Cancer Research*.

“Our findings suggest that the interaction of these two proteins is clinically important in breast cancer,” says first author Rami I. Aqeilan, research assistant professor of molecular virology, immunology and medical genetics at Ohio State's Comprehensive Cancer Center.

“The findings must be verified, but they suggest that we can use these

proteins as clinical markers that predict better survival. Therapeutically, perhaps we can design drugs or inhibitors that interact with ErbB-4 to help control the growth of these tumors.”

In 2005, a study led by the same Ohio State researchers found that the Wwox protein joins with ErbB-4 and keeps it near the cell surface. Otherwise, a fragment of ErbB4 can travel to the cell nucleus, where it activates genes involved in cancer development.

Coincidentally that same year, Finnish researchers showed that when ErbB-4 is located at the surface of breast-cancer cells, it means better survival, and when located in the cell nucleus, it indicates poor survival. In addition, they showed that, overall, the presence of ErbB4 in the cell means better survival for breast-cancer patients.

The Ohio State researchers then collaborated with the Finnish group for the present study to learn if Wwox and its partner ErbB-4 together are associated with better survival in breast-cancer patients.

The investigators analyzed tiny disks of breast-cancer tissue from 556 patients for the Wwox protein. The same samples had been analyzed previously by the Finnish group for the presence of the ErbB4 protein.

About half of the tumors showed absent or reduced levels of the Wwox protein. The cases with the protein showed better survival compared with those without it, particularly in tumors that lacked hormone receptors.

For example, of patients whose tumors were missing estrogen receptors (i.e., ER-negative tumors) and who had Wwox, nearly 70 percent were alive after 10 years vs. about 55 percent of patients of ER-negative tumors who lacked Wwox.

Similarly, patients with tumors lacking both the progesterone hormone receptor (i.e., PR-negative tumors), and the HER2 receptor, and who also lacked Wwox, also had poorer survival.

The findings suggest that loss of Wwox is associated with an unfavorable outcome, particular in tumors that lack both hormone receptors and the HER2 receptor. These “triple-negative breast cancers” have no effective treatment and are particularly deadly. This study sheds light on the role of Wwox in these difficult breast cancers and may lead to new therapies for treating them, Aqeilan says.

Last, the researchers looked at tumors with and without Wwox and with ErbB-4 at the cell surface. Of the patients in this group with Wwox, more than 90 percent were alive after 10 years, vs. about 60 percent of those without Wwox.

“Altogether, our findings suggest that the presence of Wwox probably holds ErbB-4 on the cell surface, and that this means a good prognosis for breast-cancer patients.”

Source: Ohio State University Medical Center

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