

Vaccine for HER2+ breast cancer

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Vaccine against HER2-positive breast cancer offers complete protection in lab

Researchers at Wayne State University, USA, have tested a breast cancer vaccine they say completely eliminated HER2-positive tumours in mice - even cancers resistant to current anti-HER2 therapy - without any toxicity.

The study, reported in the September 15 issue of *Cancer Research*, suggests the vaccine could treat women with HER2-positive, treatment-resistant cancer or help prevent cancer recurrence. The researchers also say it might potentially be used in cancer-free women to prevent initial development of these tumours.

HER2 receptors promote normal cell growth, and are found in low amounts on normal breast cells. But HER2-positive breast cells can contain many more receptors than is typical, promoting a particularly aggressive type of tumour that affects 20 to 30 percent of all breast cancer patients. Therapies such as trastuzumab and lapatinib, designed to latch on to these receptors and destroy them, are a mainstay of treatment for this cancer, but a significant proportion of patients develop a resistance to them or cancer metastasis that is hard to treat.

This treatment relied on activated, own-immunity to wipe out the cancer, says the study's lead investigator, Wei-Zen Wei, Ph.D., a professor of immunology and microbiology at the Karmanos Cancer Institute.

"The immune response against HER2-positive receptors we saw in this study is powerful, and works even in tumours that are resistant to current therapies," she said. "The vaccine could potentially eliminate the need to even use these therapies."

The vaccine consists of "naked" DNA – genes that produce the HER2 receptor – as well as an immune stimulant. Both are housed within an inert bacterial plasmid. In this study, the researchers used pulses of electricity to deliver the injected vaccine into leg muscles in mice, where the gene produced a huge quantity of HER2 receptors that activated both antibodies and killer T cells.

"While HER2 receptors are not usually seen by the immune system when they are expressed at low level on the surface of normal cells, a sudden flood of receptors alerts the body to an invasion that needs to be eliminated," Wei said. "During that process, the immune system learns to attack cancer cells that display large numbers of these receptors."

They also used an agent that, for a while, suppressed the activity of regulatory T cells, which normally keeps the immune system from over-reacting. In the absence of regulatory T cells, the immune system responded much more strongly to the vaccine. Then, when the researchers implanted HER2-positive breast tumours in the animals, the cancer was eradicated.

"Both tumour cells that respond to current targeted therapies and those that are resistant to these treatments were eradicated," Wei said. "This may be an answer for women with these tumours who become resistant to the current therapies."

Wei's lab is the first to develop HER2 DNA vaccines, and this is the second such vaccine Wei and her colleagues have tested more extensively. The first, described in a study in 1999, formed the model of a vaccine now being tested by a major Pharmaceutical company in early phase clinical trials in the U.S. and in Europe in women with HER2-positive breast cancer.

In order to ensure complete safety, Wei says the current test vaccine uses HER2 genes that are altered so that they cannot be oncogenic. The receptors produced do not contain an "intracellular domain" – the part of the receptor that is located just below the cell surface and transmits growth signals to the nucleus. The first vaccine was also safe, she says, but contained a little more of the native HER2 receptor structure. "With this vaccine, I am quite certain the receptor is functionally dead," she said.

"The greatest power of vaccination is protection against initial cancer development, and that is our ultimate goal with this treatment," Wei said.

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