FDA-approved drugs eliminate, prevent cervical cancer in mice

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Researchers at the University of Wisconsin-Madison School of Medicine and Public Health have eliminated cervical cancer in mice with two FDA-approved drugs currently used to treat breast cancer and osteoporosis.

Published in this week's (Nov. 9) Proceedings of the National Academy of Sciences, the findings offer hope for the 500,000 women around the world who are diagnosed with cervical cancer each year. Half of them will not survive.

The drugs, which keep estrogen from working in cells, also cleared precancerous growths, or lesions, in both the cervix and vagina, and prevented the onset of cancer in mice that had the precancerous lesions.

"We have begun to test whether the drugs are as effective in treating cervical cancer in human cells as they are in our mice," says senior author Paul Lambert, of the McArdle Laboratory for Cancer Research and the UW-Madison Carbone Cancer Center.

The lab studies, which should take one or two years to complete, could be followed quickly with phase-two or phase-three clinical trials. Early phase trials would not be necessary since the drugs have already been approved for clinical use.

Lambert and his team use special mice they developed more than 20 years ago to study cervical cancer. The mice were genetically engineered to carry human papillomavirus (HPV) 16, known to be strongly

associated with cervical cancer.

HPV is also the most common sexually transmitted infection in women in the United States. While new vaccines can prevent some of the many kinds of HPV infections, they do not eliminate already-existing infections or cervical cancers or precancerous lesions arising from pre-existing infections.

"Virtually all cervical cancers in women test positive for HPV 16," says Lambert, a professor of oncology at the UW-Madison School of Medicine and Public Health.

But not everyone who becomes infected with HPV gets cervical cancer, so scientists have suspected that something else was going on.

"Since the cervix and other female reproductive organs are so responsive to estrogen, our lab and others began to focus on that hormone," Lambert says.

Sang-Hyuk Chung, a postdoctoral fellow in Lambert's lab, zeroed in on one of the two receptors that mediate estrogen function in cells — estrogen receptor (ER) alpha. He crossed his HPV mice with mice in which ER alpha had been knocked out, then gave the animals estrogen. When the mice didn't develop cervical cancer or even precancerous lesions, Chung knew that ER alpha was an essential player in the slow cancerous process.

"We then wanted to learn if drugs that interfere with the receptor and block estrogen's ability to bind to it could be used to treat or prevent cervical cancer," he says.

Chung turned to an ER alpha blocker used to treat breast cancer, fulvestrant, and tested it on the HPV-positive mice with cervical cancer.

After one month, he found that 11 of 13 mice lost all signs of cancer. But cancer remained in all the control mice that hadn't gotten the drug.

"It was amazing to see that not only was the cancer gone, but all the precancerous lesions that give rise to cancer were also gone," says Lambert.

Chung then tested a second drug, raloxifene, which is used to treat breast cancer and osteoporosis, to make sure that the first results weren't a fluke. He found the same strong, blocking effect.

Finally, the researchers gave the drugs to animals with the precancerous lesions and found that the ER alpha blockers prevented the lesions from progressing to cancer.

Lambert's team is now testing human cervical cancer cell lines to see if ER alpha blockers stop the growth of the malignant cells. The next step will be to test the drugs on tissue samples removed from women following surgery for the cervical cancer.

"We can't be sure how the science will translate from animals to humans," says Lambert, "but we have faith in our mouse model. There are many similarities in how cervical cancer develops and manifests itself in women and in mice."

Source: University of Wisconsin-Madison (news : web)