Cervical cancer and pre-cancer cervical growths require single HPV protein

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(Medical Xpress)—Human papillomavirus (HPV) has long been implicated in cervical cancer, but details of how it happens have remained a mystery. Now researchers at the University of Wisconsin-Madison have found that a single HPV protein is required for cervical cancer and even pre-cancer growths in the cervix to survive.

In anticipation of a clinical trial in humans, the scientists and their collaborators are moving quickly to test if a gene-silencing technique could cripple the protein and eliminate cervical cancer and pre-cancerous growths in specially-bred mice.

The study, appearing online in Cancer Research, is the first to show that the protein works in living animals and in pre-cancerous growths as well as full-blown cervical cancer.

Cervical cancer is relatively rare in the United States, thanks to the widespread use of Pap smears as a screening tool. But pre-cancer lesions in the cervix, called cervical inter-epithelial neoplasias, or CINs, are common.

Low-grade CINs are typically left alone because most will shrink and pose no problem. But women with high-grade CINs have a 10 percent chance of getting cervical cancer, says Dr. Paul Lambert, senior author on the paper. In addition, surgical treatment of high-grade CINs carries a risk of excessive bleeding and even infertility.

Scientists know that two HPV cancer-causing proteins, or oncoproteins—E6 and E7—are always expressed in cervical cancer. Lambert and his team at UW's McArdle Laboratory of Cancer Research conducted experiments in cultured cell lines that suggested that the oncoproteins caused cervical cancer as well as anal and head and neck cancers. The researchers also learned that E7 had a much greater ability than E6 to cause cancer.

Other studies in different types of cancers suggested that when oncoproteins were involved, they needed to work together—blocking the expression of both often led to a more effective reduction of tumors than blocking either one alone.

But Lambert, a member of the UW Carbone Cancer Center, was intrigued with E7's power.

"In thinking of treatments, we wondered in this case if we could target just one oncoprotein, the most potent one, rather than two, which could be much more complicated," he says.

Dr. Sean Jabbar and Soyeong Park in the Lambert laboratory created and bred mice in which they could control the expression of both E7 and E6. They found that when he turned off E7 but left E6 on, the cervical cancers and CINs melted away.

"This told us that E7 should be an excellent therapeutic target for HPV-associated cancers, including pre-cancerous CINs," Lambert says.

If the gene-silencing experiments that are expected to take place soon prove effective, there's a good chance that the blocking approach could be used to control the disease without surgery.

Women in developing countries might benefit greatly, Lambert adds.

"Cervical cancer is prevalent around the world in places where screening does not exist and surgery is not available," he says.

Provided by University of Wisconsin-Madison