Virus kills breast cancer cells in laboratory

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A nondisease-causing virus kills human breast cancer cells in the laboratory, creating opportunities for potential new cancer therapies, according to Penn State College of Medicine researchers who tested the virus on three different breast cancer types that represent the multiple stages of breast cancer development.

Adeno-associated virus type 2 (AAV2) is a virus that regularly infects humans but causes no disease. Past studies by the same researchers show that it promotes tumor cell death in cervical cancer cells infected with human papillomavirus. Researchers used an unaltered, naturally occurring version of AAV2 on human breast cancer cells.

"Breast cancer is the most prevalent cancer in the world and is the leading cause of cancer-related death in women," said Samina Alam, Ph.D., research associate in microbiology and immunology. "It is also complex to treat."

Craig Meyers, Ph.D., professor of microbiology and immunology, said breast cancer is problematic to treat because of its multiple stages.

"Because it has multiple stages, you can't treat all the women the same. Currently, treatment of breast cancer is dependent on multiple factors such as hormone-dependency, invasiveness and metastases, drug resistance and potential toxicities. Our study shows that AAV2, as a single entity, targets all different grades of breast cancer."

Cells have multiple ways of dying. If damage occurs in a healthy cell, the

cell turns on production and activation of specific proteins that allow the cell to commit suicide. However, in cancer cells these death pathways are often turned off, while the proteins that allow the cell to divide and multiply are stuck in the "on" position.

One way to fight cancer is to find ways to turn on these death pathways, which is what researchers believe is happening with the AAV2 virus. In tissue culture dishes in the laboratory, 100 percent of the cancer cells are destroyed by the virus within seven days, with the majority of the cell death proteins activated on the fifth day. In another study, a fourth breast cancer derived cell line, which is the most aggressive, required three weeks to undergo cell death

"We can see the virus is killing the cancer cells, but how is it doing it?" Alam said. "If we can determine which viral genes are being used, we may be able to introduce those genes into a therapeutic. If we can determine which pathways the virus is triggering, we can then screen new drugs that target those pathways. Or we may simply be able to use the virus itself."

Research needs to be completed to learn how AAV2 is killing cancer cells and which of its proteins are activating the death pathways.

According to Meyers, the cellular myc gene seems to be involved. While usually associated with cell proliferation, myc is a protein also known to promote cell death. The scientists have observed increased expression of myc close to the time of death of the breast cancer cells in the study. They report their results in a recent issue of *Molecular Cancer*.

AAV2 does not affect healthy cells. However, if AAV2 were used in humans, the potential exists that the body's immune system would fight to remove it from the body. Therefore, by learning how AAV2 targets the death pathways, researchers potentially can find ways to treat the

cancer without using the actual virus.

In ongoing studies, the Penn State researchers have also shown AAV2 can kill cells derived from prostate cancer, methoselioma, squamous cell carcinoma, and melanoma. A fourth line of breast cancer cells - representing the most aggressive form of the disease - was also studied in a mouse breast tumor model, followed by treatment with AAV2. Preliminary results show the destruction of the tumors in the mice, and researchers will report the findings of those mouse studies soon.

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