Harmless virus kills some cancers

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Six days is all it takes for a common, non-disease-causing virus to kill cervical, breast, prostate and squamous cell cancer cells in laboratory cultures, according to Penn State College of Medicine researchers.

"Our results suggest that adeno-associated virus type 2 (AAV2), which infects the majority of the population but has no known ill effects, kills multiple types of cancer cells yet has no effect on healthy cells," said Craig Meyers, Ph.D., professor of microbiology and immunology, Penn State College of Medicine, Penn State Milton S. Hershey Medical Center. "We believe that AAV2 recognizes that the cancer cells are abnormal and destroys them. This suggests that AAV2 has great potential to be developed as an anti-cancer agent."

The study was presented June 20, 2005, at the 24th annual meeting of the American Society for Virology held June 18-22 at Penn State, University Park campus.

Although the reason why remains unclear, population-based studies have shown that people who carry AAV2 tend not to develop human papillomavirus- (HPV-) associated cervical cancer. In general, AAV2 requires association with a helper virus in order to replicate. When it finds a helper virus, such as HPV, AAV2 disrupts the life cycle of the host and induces apoptosis, a type of cell death.

"Even without co-mingling with another virus, AAV2 seems to be able to infect and express itself in other types of cancer cells also disrupting their ability to survive and inducing cell death," Meyers said. "Although

we suspect it is, more studies are needed to determine if the mechanism through which AAV2 destroys cancer cells is the same."

Scientists often refer to cancer cells as deregulated, meaning they are no longer acting or communicating like normal, healthy cells. It appears that AAV2 is able to recognize cells that have undergone deregulation, infect them, express its own genes, which disrupt the host cell's life cycle and kill it.

Scientists have suspected that AAV2 has cancer-suppressing properties. In previous studies, Meyers and his team found that one of the ways AAV2 suppresses cancer is by inhibiting the normal process of DNA duplication of human papillomavirus (HPV). HPV is known to lead to cervical cancer. A second way AAV2 suppresses cancer is linked to its ability to slow cell-cycle progression by decreasing cancer cell proliferation rates and causing growth arrest.

In this study, the team first used HPV infected epithelial cells and normal human epithelial cells, which are natural hosts for both AAV2 and HPV. In cultures infected with both AAV2 and HPV, the team found that after six days, all HPV infected cells had died. Meyers then used the same approach in four types of cancer â€“ cervical, breast, prostate and squamous cell - all epithelial cell cancers. Epithelial cells are those that cover or line all of the internal and external parts of the body. No matter the type of epithelial cancer cells, when treated with AAV2, all cancer cells were dead in six days. Though previous have investigated the cancer-targeting potential of AAV2, none allowed the AAV2 to remain in culture long enough to see the effect that Meyers and his team observed.

"One of the most compelling findings is that AAV2 appears to have no pathologic effects on healthy cells," Meyers said. "So many cancer therapies are as poisonous to healthy cells as they are to cancer cells. A

therapy that is able to distinguish between healthy and cancer cells could be less difficult to endure for those with cancer."

Though similar in design and effectiveness to some gene therapies, Meyers and his team did not modify the AAV2, but left it in its natural form. Therefore, it would not be classified as a gene therapy.

Future studies will investigate the precise mechanisms through which AAV2 causes cancer cell death, and how the virus might be enhanced to more aggressively target and kill cancers.

A provisional patent application for this work was recently submitted.

Source: Penn State