Low dose of targeted drug might improve cancer-killing virus therapy

16 June 2014

Giving low doses of a particular targeted agent with additional toxicity. a cancer-killing virus might improve the effectiveness of the virus as a treatment for cancer, according to a study led by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

Viruses that are designed to kill cancer cells – oncolytic viruses – have shown promise in clinical trials for the treatment of brain cancer and other solid tumors. This cell and animal study suggests that combining low doses of the drug bortezomib with a particular oncolytic virus might significantly improve the ability of the virus to kill cancer cells during oncolytic virus therapy.

The research is published in the journal *Clinical Cancer Research*.

"These findings pave the way for a treatment strategy for cancer that combines low doses of bortezomib with an oncolytic virus to maximize the efficacy of the virus with little added toxicity," says principal investigator Balveen Kaur, PhD, professor and vice chair of research, Department of Neurological Surgery and Radiation Oncology, and a member of the OSUCCC – James Translational Therapeutics Program.

"Because bortezomib is already approved by the Food and Drug Administration, a clinical trial could be done relatively quickly to test the effectiveness of the drug-virus combination," Kaur says.

Bortezomib inhibits the activity of proteasomes, structures in cells that break down and recycle proteins. Kaur notes that blocking these "cellular recycling plants" activates a cellular stress response and increases the expression of heat shock proteins. This reaction, which can lead to bortezomib resistance, makes the cells more sensitive to oncolytic virus therapy with little

For this study, Kaur and her colleagues used a herpes simplex virus-type 1 oncolytic virus. Key technical findings include:

- One of the overexpressed heat-shock proteins, HSP90, facilitates oncolytic virus replication, enabling the virus to kill more tumor cells;
- In a glioma model, the combination treatment suppressed tumor growth by 92 percent relative to controls and improved survival (six of eight tumors had completely regressed by day 23 after treatment);
- Similar outcomes occurred in a head and neck cancer model.

"To our knowledge, this study is the first to show synergy between an oncolytic HSV-1-derived cancer killing virus and bortezomib," Kaur says. "It offers a novel therapeutic strategy that can be rapidly translated in patients with various solid tumors."

More information: clincancerres.aacrjournals.org … CCR-14-0553.abstract

Provided by Ohio State University Medical Center