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Oncolytic reovirus combined with trastuzumab enhances antitumor efficacy through TRAIL signaling in human HER2-positive gastric cancer cells

BACKGROUND :
Human epidermal growth factor receptor 2 (HER2) overexpression and amplification have been detected in 10% to 20% of gastric cancers and are associated with a poor outcome. The HER2-targeting agent, trastuzumab, is effective for HER2-overexpressing gastric cancer therapy. As oncolytic reovirus is currently undergoing clinical trials internationally, we wanted to explore whether the combination therapy using trastuzumab and reovirus might provide a novel, more effective therapeutic option for gastric cancer.

METHODS:
Cell proliferation and cell apoptosis were examined *in vitro*, while molecular analysis of pathways responsible for cell damage was examined using polymerase chain reaction array. Activation of the proteins related to apoptosis, cell growth and survival was detected by Western blotting. Mouse tumor xenograft models were used to examine antitumor activity *in vivo*.

RESULTS:
Both *in vitro* and *in vivo* studies provided evidence that the combination therapy is a more powerful modality against HER2-overexpressing gastric cancer cells than treatment using a single agent. Molecular analysis indicated that the combination therapy induced significantly higher levels of tumor necrosis factor related apoptosis-inducing ligand (TRAIL) in cancer cells. Antibody against TRAIL strongly inhibited cell toxicity caused by the combined treatment.

CONCLUSIONS:
These results suggest that reovirus may augment trastuzumab-induced cytotoxicity in gastric cancer cells.