

Combination of Vaccinia Virus and Semliki Forest Virus Encoding a Foreign Antigen to Treat Ovarian Cancer

Yu-Qian Zhang and Chien-Fu Hung

Vaccinia virus (VV) and Semliki Forest virus (SFV) are oncolytic viruses which have been shown to infect and kill tumor cells. It has also been demonstrated that, when given intraperitoneally, these viruses preferentially infect ovarian tumor cells but not normal tissue, suggesting that oncolytic therapy with SFV or VV is a promising strategy for ovarian cancer treatment. A concern about this strategy is these viruses may infect only a portion of tumor cells *in vivo*, however, the generation of neutralizing antibodies specific to these viruses would prevent the repeated treatment.

By using a mouse ovarian tumor model, we demonstrated that infection by SFV or VV inhibits the subsequent infection by the same virus, and combination treatments with SFV and VV display increased anti-tumor effects comparing with the repeated treatments. Combination infections by SFV and VV both encoding an immunogenic foreign antigen ovalbumin (OVA) induce potent T cell response against OVA, which, potentially, could kill infected tumor cells presenting OVA antigen.

To evaluate the anti-tumor effects of combination treatments with SFV and VV both encoding OVA, we performed peritoneal wash and detected a large number of OVA specific T cells in the peritoneal cavity, which result in the killing of mouse ovarian tumor cells infected by VV encoding OVA *in vitro*. And combination treatments with SFV and VV both encoding OVA generate enhanced anti-tumor effects than combination treatments with wild type SFV and VV in the mouse ovarian tumor model.

Taken together, SFV and VV combination treatments display enhanced anti-tumor effects than the repeated treatments with the same virus, and treatments with SFV and VV encoding a foreign antigen further increase the anti-tumor activity through both viral oncolysis and tumor-specific immunity. This study provides a novel strategy for the treatment of ovarian cancer.