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Herpes Simplex Virus Oncolytic Viral Immunotherapy Against Colorectal Cancer

Immunotherapeutic approaches to the treatment of cancer include immune checkpoint inhibitor (ICIs), monoclonal antibodies (mAbs), cancer vaccines, and adoptive cellular therapies (ACTs). Despite great success, these cancer treatment options still face many challenges such as a low response rate and serious side effects. Oncolytic viral immunotherapy (OViT), whereby viruses with the ability to selectively infect tumor cells and induce antitumor immune responses, are used for cancer treatment. Talimogene laherparevec (T-VEC) is the first FDA approved virus for patients with advance melanoma. The approval of T-VEC demonstrates the therapeutic potential and safety of OViT. However, beyond melanoma, the efficacy of T-VEC against other cancer types is not fully understood.

We sought to investigate the anti-cancer effect of a mouse version T-VEC against colorectal cancer CT26 cells. Colorectal cancer is the second leading cause of cancer death in the U.S. The mouse version of T-VEC herein called HSV-1 ΔICP34.5 mGM-CSF ΔICP47, was constructed using the two-step double-red recombination protocol using the HSV-1(F) viral genome cloned as a bacterial artificial chromosome (BAC). The virus is engineered in a similar manner as T-VEC, with the exception that the human granulocyte macrophage colony stimulating factor (GM-CSF) gene is replaced with mouse GM-CSF. When we examined the plaque morphology of the two viruses, we observed that plaques of the HSV-1 ΔICP34.5 mGM-CSF ΔICP47 virus were indistinguishable from wild type-plaques. Next, we investigated the cytolytic activity of HSV-1 ΔICP34.5 mGM-CSF ΔICP47 virus against CT26 cancer cells *in vitro*. HSV-1 ΔICP34.5 mGM-CSF ΔICP47 killed more than 70% of the CT26 cells when infected at an MOI of 0.1 or 1 (3 days post-infection). This result suggests that virus can replicate and may induce anti-cancer immune response against CT26 *in vivo*.