Armed Myxoma Virus Demonstrates Efficacy in Syngeneic Tumor Models Alone and in Combination with Immune Checkpoint Inhibitors

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Abstract 406

BACKGROUND

Oncolytic viruses (OV) selectively replicate in and lyse tumor cells and provide stimulation to the immune system. This represents a promising therapeutic option for cancer patients that do not respond well to treatment with immune checkpoint inhibitors. Myxoma virus (MYXV) is a member of the Poxviridae family of double stranded DNA viruses. The natural host of MYXV is a subset of lagomorphs, but MYXV can infect cancer cell lines of humans and other species. The genome of MYXV is relatively large and is amenable to engineering for expression of transgenes making it an excellent oncolytic virus for introduction of immunomodulatory proteins. The current work describes the oncolytic activity, transgene production capability, in vivo activity and immunomodulatory mechanism of actions following intratumoral (IT) and intravenous (IV) administration of armed myxoma viruses in murine cancer models.

Oncolytic Virus

Myxoma

Arming

MYXOMA VIRUS INFECTS MOUSE CANCER CELLS

Figure 1. Myxoma virus infects a variety of mouse cancer cell lines in vitro

The indicated mouse tumor cell lines were infected with myxoma virus containing transgenic GFP (MYXV-GFP) at multiplicity of infection (MOI) = 1 and incubated for 24 hours in vitro. Following incubation photographs of the cells under light (left panel) or fluorescent (middle panels) microscopy. Overlay images (right panel) are also shown.

Light

GFP

Overlay

Figure 2. Multi-armed myxoma virus is efficacious in multiple tumor models following intratumoral or intravenous delivery in the presence or absence of immune checkpoint inhibition

Conclusions

Myxoma is a large dsDNA pox virus suitable for oncolytic virotherapy, is engineered to carry multiple transgenic payloads, and is not pathogenic to humans. Multi-armed myxoma demonstrates efficacy in multiple subcutaneous and metastatic syngeneic tumor models following intratumoral or intravenous delivery and combinatorial efficacy with immune checkpoint inhibitors.

Evidence of modulation of tumor infiltrating lymphocytes populations to favor anti-tumor immunity including increased CD8/Treg and M1/M2 macrophage ratios

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