Abstract 406

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

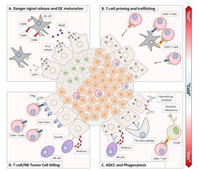
Lina S. Franco, Lino E. Torres-Dominguez, Joseph Mamola, Ana L. de Matos, Mario Abrantes, Benjamin S. Walker, Zach Tacner, Cassandra Kien, Natalie M. Elliott, Wazir Abdullahi, Grant McFadden, Leslie L. Sharp OncoMyx Therapeutics, 445 N. Fifth St. Phoenix AZ 85004

OncoMyx Therapeutics

BACKGROUND

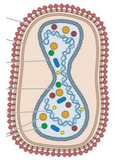
Oncolytic viruses (OV) selectively replicate in and lyse tumor cells and provide stimulation to the immune system. This represents a promising therapeutic option for cancer patients that do not respond well to treatment with immune checkpoint inhibitors. Myxoma virus (MYXV) is a member of the Poxviridae 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

Oncolytic Virus



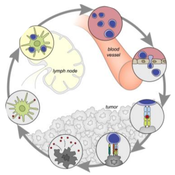
Oncolytic Viruses:
- Kill cancer cells directly
- Release tumor antigens
- Promote inflammation to turn cold tumors hot

Myxoma



Myxoma is a rabbit pox virus:
- Large, dsDNA allows engineering of multiple payload genes
- Not pathogenic to humans
- Suitable for IV delivery

Arming



Arming selected that:
- Target additional points around cancer immunity cycle
- Complementary to approved immune checkpoint inhibitors

MYXOMA VIRUS INFECTS MOUSE CANCER CELLS

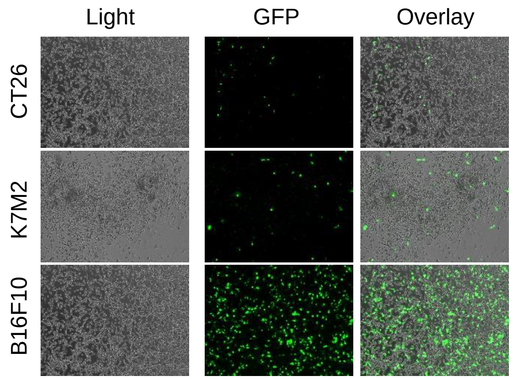


Figure 1. Myxoma virus infects a variety of mouse cancer models in vitro

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.

MULTI-ARMED MYXOMA IS EFFICACIOUS IN SYNGENEIC MODELS FOLLOWING IT OR IV DELIVERY ± ICI

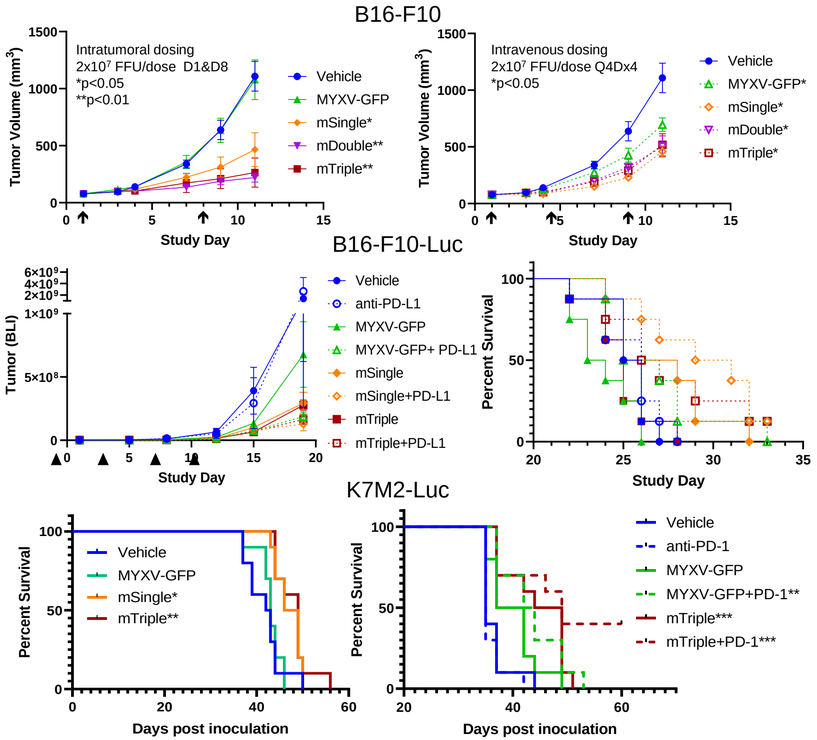


Figure 2. Multi-armed myxoma virus is efficacious in multiple tumor models following intratumoral or intravenous delivery in the presence or absence of immune checkpoint inhibitors (ICI)

Top Panel: B16-F10 cells were implanted subcutaneously. Tumors were randomized when the mean tumor volume was ~85mm^3 (Study Day 1). Animals were injected with vehicle control or 2x10^7 FFU/dose of the indicated virus intratumorally (IT) on Day 1 and Day 8 (left panel) or intravenously (IV) once every four days for four doses (Q4Dx4).

Middle Panel: B16-F10-Luc cells were implanted IV via tail vein injection (Study Day 1). Animals were injected with vehicle control or 2x10^7 FFU/dose of the indicated virus IV once every four days for four doses (Q4Dx4) Anti-PD-L1 was injected intraperitoneally (IP) at 10 mg/kg Q4Dx4 beginning 3 days following tumor inoculation. Bioluminescence imaging was recorded on the indicated days (left). Animals were followed until they met IACUC survival endpoints (right).

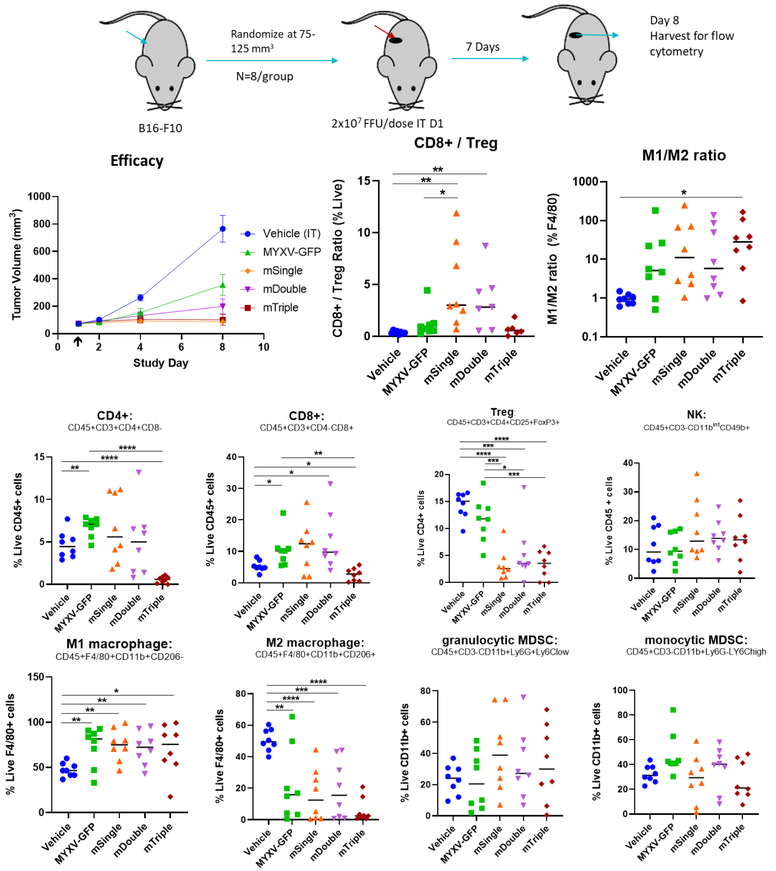
Lower Panel: K7M2-Luc cells were implanted intravenously via tail vein injection (Study Day 1). Animals were injected with vehicle control or 2x10^7 FFU/dose of the indicated virus IV and/or anti-PD-1 injected IP at 10 mg/kg Q4Dx4 beginning 3 days following tumor inoculation. Animals were followed until they met IACUC survival endpoints (right).

Figure 3. Multi-armed myxoma virus alters the tumor infiltrating lymphocyte profile in B16-F10 tumors

B16-F10 cells were implanted subcutaneously. Tumors were randomized when the mean tumor volume was ~85mm^3 (Study Day 1). Animals were injected with vehicle control or 2x10^7 FFU/dose of the indicated virus IT on Day 1. Tumors were measured and collected 7 days following IT injection, digested to release infiltrating lymphocytes, and stained for the indicated lymphocyte markers.

In vivo studies were performed by Translational Drug Development (TD2) or Arizona State University and were governed by the corresponding IACUC protocols. Special thanks to Jessica Dalsing-Hernandez at TD2.

MULTI-ARMED MYXOMA INCREASES ANTI-TUMOR INFILTRATING LYMPHOCYTE POPULATIONS



CONCLUSIONS

Myxoma is a large dsDNA pox virus suitable for oncolytic virotherapy, is engineerable 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

DO NOT POST