CLAIMS

We claim:

1. An engineered myxoma virus (MYXV) comprising a transgene encoding one or more immunomodulatory proteins.

2. The engineered MYXV of claim 1, wherein the one or more immunomodulatory proteins is Stimulator of interferon genes (STING), interleukin-12 (IL-12), Fusion-associated small transmembrane (FAST), an immune checkpoint inhibitor, a tumor necrosis factor (TNF) protein, or a combination thereof.

3. The engineered MYXV of claim 2, wherein the IL-12 is an IL-12A.

4. The engineered MYXV of claim 2, wherein the IL-12 is an IL-12B.

5. The engineered MYXV of claim 2, wherein the immune checkpoint inhibitor is a PD-L1 binding molecule.

6. The engineered MYXV of claim 5, wherein the PD-L1 binding molecule is an anti-PD-L1 antibody or an antigen-binding fragment thereof.

7. The engineered MYXV of any one of claims 1-6, wherein the one or more immunomodulatory proteins is capable of stimulating a toll like receptor (TLR), activating Nuclear factor-κB **(**NF-κB), or activating an interferon regulatory factor (IRF).

8. The engineered MYXV of any one of claims 1-7, wherein the engineered MYXV comprises a modification at or adjacent to one or more genes selected from the group consisting of M001R, M002R, M003.1R, M003.2R, M004.1R, M004R, M005R, M006R, M007R, M008.1R, M008R, M009L, M013, M036L, M063L, M11L, M128L, M131R, M135R, M136R, M141R, M148R, M151R, M152R, M153R, M154L, M156R, M-T2, M-T4, M-T5, M-T7, and SOD.

9. The engineered MYXV of any one of claims 1-8, wherein the engineered MYXV comprises a modification at or adjacent to M011L, M063, M135R, M136R, M-T2, M-T4, M-T5, M-T7 or SOD.

10. The engineered MYXV of claim 8 or claim 9, wherein the modification comprises a deletion or an insertion.

11. The engineered MYXV of any one of claims 8-10, wherein the transgene replaces a portion of M011L, M063, M135R, M136R, M-T2, M-T4, M-T5, M-T7, or SOD.

12. The engineered MYXV of any one of claims 8-11, wherein the transgene is located between the M135R and M136R genes of the genome of the MYXV.

13. The engineered MYXV of any one of claims 8-12, wherein the transgene replaces a portion of M135R.

14. The engineered MYXV of any one of claims 8-13, wherein the engineered MYXV is an M135R knockout.

15. The engineered MYXV of any one of claims 8-11, wherein engineered MYXV is a SOD knockout.

16. The engineered MYXV of any one of claims 1-15, further comprising a reporter gene.

17. The engineered MYXV of claim 15, wherein the reporter gene encodes a fluorescent protein, a luminescent substrate or an enzyme.

18. The engineered MYXV of any one of claims 1-17, wherein the engineered MYXV increases autophagy in infected cells by at least 5% compared to a MYXV that lacks the transgene as determined by an LC3-I to LC3-II conversion assay.

19. The engineered MYXV of any one of claims 1-18, wherein the engineered MYXV increases killing of infected cancer cells by at least 5% compared to a MYXV that lacks the transgene as determined by an *in vitro* flow cytometric assay.

20. The engineered MYXV of any one of claims 1-19, wherein the engineered MYXV increases killing of uninfected cancer cells by at least 5% compared to a MYXV that lacks the transgene as determined by an *in vitro* flow cytometric assay.