

CLAIMS

What is claimed is:

1. A myxoma virus (MYXV) comprising a transgene that encodes a multi-specific immune cell engager.
2. The MYXV of claim 1, wherein the multi-specific immune cell engager comprises a Bi-specific Natural Killer and Neutrophil engager (BiKE), a Bi-specific T Cell Engager (BiTE), or a membrane-integrated T cell engager (MiTE).
3. The MYXV of claim 1 or claim 2, wherein the multi-specific immune cell engager binds to an antigen present on a hematologic cancer cell.
4. The MYXV of claim 3, wherein the hematologic cancer cell is a myeloma cell, a leukemia cell, or a lymphoma cell.
5. The MYXV of claim 2, wherein the BiKE binds to an antigen present on a natural killer cell or a neutrophil.
6. The MYXV of claim 2, wherein the BiTE binds to an antigen present on a T cell.
7. The MYXV of claim 2, wherein the MiTE binds to an antigen present on a T cell.
8. The MYXV of any one of claims 2-7, wherein the BiKE binds to CD16 or CD138.
9. The MYXV of any one of claims 2-8, wherein the BiKE binds to CD16 and CD138.
10. The MYXV of any one of claims 2-8, wherein the BiTE binds to CD3 or CD138.
11. The MYXV of any one of claims 2-8, wherein the BiTE binds to CD3 and CD138.
12. The MYXV of any one of claims 2-8, wherein MiTE binds to CD3 or CD138.
13. The MYXV of any one of claims 2-8, wherein MiTE binds to CD3 and CD138.
14. The MYXV of any one of claims 1-13, wherein the multi-specific immune cell engager comprises one or more single chain variable fragments (scFvs) derived from an anti-human CD antibody.
15. The MYXV of any one of claims 1-13, wherein the multi-specific immune cell engager comprises one or more humanized single chain variable fragments (scFvs).

16. The MYXV of any one of claims 2-15, wherein the BiKE comprises a sequence that is at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99%, or 100% identical to any one of SEQ ID NOs: 4-21.
17. The MYXV of any one of claims 2-15, wherein the BiTE comprises a sequence that is at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99%, or 100% identical to any one of SEQ ID NOs: 6, 7, 10-15, or 32-39.
18. The MYXV of any one of claims 2-15, wherein the MiTE comprises a sequence that is at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99%, or 100% identical to any one of SEQ ID NOs: 6, 7, 10-15, or 32-39.
19. The MYXV of any one of claims 1-18, wherein the transgene is located between the M135 gene and M136 gene of the genome of the MYXV.
20. The MYXV of any one of claims 1-19, further comprising a reporter gene.
21. The MYXV of claim 20, wherein the reporter gene encodes a fluorescent protein.
22. The MYXV of claim 20, wherein the reporter gene encodes a luminescent substrate or an enzyme.
23. The MYXV of any one of claims 1-22, further comprising a mutation in the genome of the MYXV.
24. The MYXV of claim 23, wherein the mutation is present in 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.
25. The MYXV of claims 23 or claim 24, wherein the mutation is a deletion.
26. The MYXV of claim 25, wherein the deletion deletes at least a portion of M135R.
27. The MYXV of any one of claims 1-26, wherein the 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.

28. The MYXV of any one of claims 1-27, wherein the 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.
29. A composition comprising the MYXV of any one of claims 1-28 and a pharmaceutically acceptable carrier.
30. A method of treating a hematological cancer in a subject in need thereof, comprising administering to the subject the MYXV of any one of claims 1-28 or the composition of claim 29.
31. The method of claim 30, wherein the subject is a human.
32. The method of claim 30 or claim 31, wherein the MYXV is capable of infecting cells that have a deficient innate anti-viral response.
33. The method of any one of claims 30-32, wherein the MYXV is capable of infecting cancer cells.
34. The method of any one of claims 30-33, wherein the hematological cancer is a myeloma, multiple myeloma, leukemia, or lymphoma.
35. A method of treating a hematological cancer in a subject in need thereof, comprising administering to the subject a leukocyte, wherein the leukocyte comprises or is associated with the MYXV of any one of claims 1-28.
36. The method of claim 35, further comprising adsorbing the MYXV *ex vivo* onto a surface of the leukocyte.
37. The method of claim 36, wherein the adsorbing the MYXV onto the surface of the leukocyte comprises exposing the leukocyte to the MYXV under conditions that permit binding of the MYXV to the surface of the leukocyte.
38. The method of claim 36 or claim 37, wherein the adsorbing comprises exposing the leukocyte to the MYXV for at least five minutes.
39. The method of claim 36 or claim 37, wherein adsorbing comprises exposing the leukocyte to the MYXV for about one hour.

40. The method of any one of claims 36-39, wherein the adsorbing comprises exposing the leukocyte to the MYXV at a multiplicity of infection (MOI) of between about 0.001 and 1000.
41. The method of any one of claims 36-39, wherein the adsorbing comprises exposing the leukocyte to the MYXV at a multiplicity of infection (MOI) of between about 0.1 and 10.
42. The method of any one of claims 36-41, wherein the leukocyte is obtained from peripheral blood.
43. The method of any one of claims 36-42, wherein the leukocyte is obtained from bone marrow.
44. The method of any one of claims 36-42, wherein the leukocyte is a peripheral blood mononuclear cell.
45. The method of any one of claims 36-44, wherein the leukocyte is obtained from the subject's tissue.
46. The method of any one of claims 36-44, wherein the leukocyte is obtained from a donor's tissue that is HLA-matched, HLA-mismatched, haploidentical, or a combination thereof relative to the subject.
47. The method of any one of claims 36-46, wherein the leukocyte is formulated in a pharmaceutical composition.
48. The method of any one of claims 36-47, wherein the leukocyte is administered systemically.
49. The method of any one of claims 36-47, wherein the leukocyte is administered parenterally.
50. The method of any one of claims 36-47, wherein the leukocyte is administered intravenously.