

CLAIMS

1. A composition comprising a polyclonal population of cytotoxic T-lymphocytes (CTLs) that recognize a plurality of viral antigens, wherein the plurality of viral antigens comprise at least one first antigen from PIV and at least one second antigen from one or more second viruses.
2. The composition of claim 1, wherein the CTLs are generated by contacting peripheral blood mononuclear cells (PBMCs) with a plurality of pepmix libraries, each pepmix library comprising a plurality of overlapping peptides spanning at least a portion of a viral antigen, wherein at least one of the plurality of pepmix libraries spans a first antigen from PIV-3 and wherein at least one additional pepmix library of the plurality of pepmix libraries spans each second antigen.
3. The composition of claim 1, wherein the CTLs are generated by contacting T cells with dendritic cells (DCs) primed with a plurality of pepmix libraries, each pepmix library comprising a plurality of overlapping peptides spanning at least a portion of a viral antigen, wherein at least one of the plurality of pepmix libraries spans a first antigen from PIV-3 and wherein at least one additional pepmix library of the plurality of pepmix libraries spans each second antigen.
4. The composition of claim 1, wherein the CTLs are generated by contacting T cells with dendritic cells (DCs) nucleofected with at least one DNA plasmid encoding the PIV-3 antigen and at least one DNA plasmid encoding each second antigen.
5. The composition of claim 4, wherein the plasmid encodes at least one PIV-3 antigen and at least one of the second antigens.
6. The composition of any one of claims 1-5, comprising CD4⁺ T-lymphocytes and CD8⁺ T- lymphocytes.
7. The composition of any one of claims 1-6, comprising CTLs expressing $\alpha\beta$ T cell receptors.
8. The composition of any one of claims 1-7, comprising MHC-restricted CTLs.

9. The composition of any one of claims 1-8, wherein the one or more second viruses is selected from the group consisting of respiratory syncytial virus (RSV), Influenza, human metapneumovirus (hMPV), and a combination thereof.
10. The composition of any one of claims 1-9, wherein the one or more second viruses comprises respiratory syncytial virus (RSV), Influenza, human metapneumovirus, or a combination thereof.
11. The composition of any one of claims 1-9, wherein the one or more second viruses consists of respiratory syncytial virus (RSV), Influenza, human metapneumovirus, or a combination thereof.
12. The composition of any one of claims 1-11, comprising 1, 2, 3, or 4 first antigens.
13. The composition of claim 12, wherein the first antigen is selected from the group consisting of PIV-3 antigen M, PIV-3 antigen HN, PIV-3 antigen N, PIV-3 antigen F, and a combination thereof.
14. The composition of claim 12, comprising the following 4 first antigens: PIV-3 antigen M, PIV-3 antigen HN, PIV-3 antigen N, and PIV-3 antigen F.
15. The composition of any one of the preceding claims, comprising two or three second viruses.
16. The composition of any one of the preceding claims, comprising three second viruses.
17. The composition of claim 16, wherein the three second viruses are influenza, RSV, and hMPV.
18. The composition of any one of claims 1-17, comprising at least two second antigens per each second virus.
19. The composition of any one of claims 1-17, comprising 1, 2, 3, 4, 5, 6, 7, or 8 second antigens.
20. The composition of any one of claims 1-19, wherein the second antigen is selected from the group consisting of influenza antigen NP1, influenza antigen MP1, RSV antigen N,

- RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, hMPV antigen N, and a combination thereof.
21. The composition of claim 19, wherein the second antigen comprises influenza antigen NP1, influenza antigen MP1, or both.
 22. The composition of claim 19, wherein the second antigen comprises RSV antigen N, RSV antigen F, or both
 23. The composition of claim 19, wherein the second antigen comprises hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, hMPV antigen N, and combinations thereof.
 24. The composition of claim 19, wherein the second antigen comprises each of influenza antigen NP1, influenza antigen MP1, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, and hMPV antigen N.
 25. The composition of any one of claims 1-8, wherein the plurality of antigens comprise PIV-3 antigen M, PIV-3 antigen HN, PIV-3 antigen N, PIV-3 antigen F, influenza antigen NP1, influenza antigen MP1, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, and hMPV antigen N.
 26. The composition of any one of claims 1-8, wherein the plurality of antigens consist of, or consist essentially of, PIV-3 antigen M, PIV-3 antigen HN, PIV-3 antigen N, PIV-3 antigen F, influenza antigen NP1, influenza antigen MP1, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, and hMPV antigen N.
 27. The composition of any one of claims 1-26, wherein the CTLs are cultured *ex vivo* in the presence of both IL-7 and IL-4.
 28. The composition of any one of claims 1-27, wherein the multivirus CTLs have expanded sufficiently within 9-18 days of culture such that they are ready for administration to a patient.
 29. The composition of any one of claims 1-28, wherein the CTLs exhibit one or more properties selected from:
 - a. negligible alloreactivity;

- b. less activation induced cell death of antigen-specific T cells harvested from a patient than corresponding antigen-specific T cells harvested from the same patient, but not cultured in the presence of both IL-7 and IL-4; and
 - c. viability of greater than 70%.
- 30. The composition of any one of claims 1-29, wherein the composition is negative for bacteria and fungi for at least 7 days in culture; exhibit less than 5 EU/ml of endotoxin, and are negative for mycoplasma.
- 31. The composition of any one of claims 1-30, wherein the pepmixes were chemically synthesized and are, optionally >90% pure.
- 32. The composition of any one of claims 1-31, wherein the CTLs are Th1 polarized.
- 33. The composition of any one of claims 1-32, wherein the CTLs are able to lyse viral antigen-expressing targets cells.
- 34. The composition of any one of claims 1-33, wherein the CTLs do not significantly lyse non-infected autologous or allogenic target cells.
- 35. A pharmaceutical composition comprising the composition of any one of claims 1-34 formulated for intravenous delivery, wherein the composition is negative for bacteria and fungi for at least 7 days in culture; exhibit less than 5 EU/ml of endotoxin, and are negative for mycoplasma.
- 36. A method of lysing a target cell comprising contacting the target cell with the composition of any one of claims 1-34 or the pharmaceutical composition of claim 35 *in vitro*.
- 37. Use of the composition of any one of claims 1-34 or the pharmaceutical composition of claim 35, in the manufacture of a medicament for lysing a target cell, wherein the medicament is to be contacted with the target cell *in vivo* in a subject.
- 38. The use of claim 37, wherein the contacting occurs *in vivo* via administration of the CTLs to a subject.

39. Use of the composition of any one of claims 1-34 or the pharmaceutical composition of claim 35, in the manufacture of a medicament for treating or preventing a viral infection in a subject in need thereof.
40. The use of claim 38 or 39, wherein between 5×10^6 and 5×10^7 CTL / m^2 is to be administered to the subject.
41. The use of any one of claims 38-40, wherein the subject is immunocompromised.
42. The use of any one of claims 38-41, wherein the subject has acute myeloid leukemia, acute lymphoblastic leukemia, or chronic granulomatous disease.
43. The use of any one of claims 38-42, wherein the subject, prior to receiving the CTLs, received:
- a. a matched related donor transplant with reduced intensity conditioning;
 - b. a matched unrelated donor transplant with myeloablative conditioning;
 - c. a haplo-identical transplant with reduced intensity conditioning; or
 - d. a matched related donor transplant with myeloablative conditioning.
44. The use of any one of claims 38-40, wherein the subject
- a. has received a solid organ transplantation;
 - b. has received chemotherapy;
 - c. has an HIV infection;
 - d. has a genetic immunodeficiency; and/or
 - e. has received an allogeneic stem cell transplant.
45. The use of any one of claims 38-44, wherein the composition is to be administered to the subject a plurality of times.
46. The use of any one of claims 38-45, wherein the administration of the composition effectively treats or prevents a viral infection in the subject, wherein the viral infection is

selected from the group consisting of parainfluenza virus type 3, respiratory syncytial virus, Influenza, and human metapneumovirus.

47. The use of any one of claims 38-46, wherein the subject is a human.
48. A composition comprising a polyclonal population of cytotoxic T-lymphocytes (CTLs) that recognize a plurality of viral antigens, wherein the plurality of viral antigens comprise at least one antigen selected from parainfluenza virus type 3 (PIV-3), respiratory syncytial virus, Influenza, and human metapneumovirus.
49. The composition of claim 48, comprising a polyclonal population of cytotoxic T-lymphocytes (CTLs) that recognize a plurality of viral antigens, wherein the plurality of viral antigens comprise at least one antigen from each of parainfluenza virus type 3, respiratory syncytial virus, Influenza, and human metapneumovirus.
50. The composition of claim 48, comprising a polyclonal population of cytotoxic T-lymphocytes (CTLs) that recognize a plurality of viral antigens, wherein the plurality of viral antigens comprise at least two antigen from each of parainfluenza virus type 3, respiratory syncytial virus, Influenza, and human metapneumovirus.
51. The composition of any one of claims 48-50, wherein the plurality of antigens comprise, consist of, or consist essentially of, PIV-3 antigen M, PIV-3 antigen HN, PIV-3 antigen N, PIV-3 antigen F, influenza antigen NP1, influenza antigen MP1, RSV antigen N, RSV antigen F, hMPV antigen M, hMPV antigen M2-1, hMPV antigen F, and hMPV antigen N.
52. A pharmaceutical composition comprising the composition of any one of claims 48-51 formulated for intravenous delivery.
53. The pharmaceutical composition of claim 52, wherein the composition is negative for bacteria and fungi for at least 7 days in culture; exhibit less than 5 EU/ml of endotoxin, and are negative for mycoplasma.
54. A method of lysing a target cell comprising contacting the target cell with the composition of any one of claims 48-51 or the pharmaceutical composition of claim 52 *in vitro*.

55. Use of the composition of any one of claims 48-51 or the pharmaceutical composition of claim 52, in the manufacture of a medicament for lysing a target cell, wherein the medicament is to be contacted with the target cell *in vivo* in a subject.
56. The use of claim 55, wherein the contacting occurs *in vivo* via administration of the CTLs to a subject.
57. Use of the composition of any one of claims 48-51 or the pharmaceutical composition of claim 52, in the manufacture of a medicament for treating or preventing a viral infection in a subject in need thereof.
58. The use of any one of claims 55-57, wherein the composition is to be administered to the subject a plurality of times.
59. The use of any one of claims 55-58, wherein the administration of the composition effectively treats or prevents a viral infection in the subject, wherein the viral infection is selected from the group consisting of parainfluenza virus type 3, respiratory syncytial virus, Influenza, and human metapneumovirus.
60. The use of any one of claims 55-59, wherein the subject is a human.