

CLAIMS

1. An NK cell expanding composition comprising a membrane bound inverted Fc domain bound to an external surface of a feeder cell, an engineered PM particle, or an exosome.
2. The NK cell expanding composition of claim 1, comprising the engineered PM particle or engineered exosome substantially free of feeder cells.
3. The NK cell expanding composition of claim 2, wherein the engineered PM particle further comprises at least one NK cell effector agent.
4. The NK cell expanding composition of claim 1, further comprising at least one NK cell effector agent.
5. The NK cell expanding composition of claim 3 or 4, wherein the at least one NK cell effector agent is IL-21 or IL-15.
6. The NK cell expanding composition of claim 5, further comprising a second NK cell effector agent, wherein the second NK cell effector agent is 41 BBL.
7. The NK cell expanding composition of claim 1, wherein the engineered PM particle comprises a plasma membrane vesicle or an exosome purified from NK cell feeder cells transfected or transduced with a fusion protein comprising a transmembrane domain linked to an Fc domain, and at least one NK cell effector agent.
8. The NK cell expanding composition of claim 6, further comprising at least one additional NK cell effector agent, wherein the at least one additional NK cell effector agent is a cytokine, an adhesion molecule, or an NK cell activating agent; wherein the at least one additional NK cell effector agent is selected from IL-15, IL-2, IL-12, IL-18, IL- 21 , MICA, UBLP, 2sB4, LFA-1, a Notch ligand, ligands for NKp46, or BCM1/SLAMF2, TLR ligands, and NKG2D ligands.

9. An NK cell composition comprising an in vitro NK cell population in contact with the NK cell expanding composition of claim 1.
10. An expanded population of NK cells exposed in vitro to an NK cell expanding composition, the composition comprising feeder cells, or comprising at least one engineered PM particle and being free of feeder cells, wherein the feeder cells or engineered PM particle comprise an Fc domain bound to an external surface thereof.
11. The expanded population of NK cells of claim 10, wherein the NK cells have increased cytotoxicity compared to non-expanded NK cells.
12. A composition comprising a therapeutic dose of NK cells comprising the expanded population of NK cells of claim 10 or 11, and a pharmaceutically acceptable carrier.
13. A method of treating, ameliorating, reducing, and/or inhibiting a cancer or metastasis or an infectious disease in a subject comprising administering to the subject in need thereof an effective amount of the expanded population of NK cells of claim 10 or 11 or the composition of claim 12.
14. The method of claim 13, wherein the cancer is selected from the group consisting of a tumor, a hematologic cancer, a lymphoma, a leukemia, acute myeloid leukemia, myelodysplastic syndrome, chronic myeloid leukemia, acute lymphoblastic leukemia, myelofibrosis, multiple myeloma, a colorectal cancer, a colon cancer, lung cancer, a head and neck cancer, ovarian cancer, pancreatic cancer, liver cancer, skin cancer, prostate cancer, kidney cancer, intraperitoneal cancer, and breast cancer.
15. A method of inhibiting, reducing, and/or preventing cancer or metastasis recurrence before or after stem cell transplant comprising administering to a subject in need thereof an effective amount of the expanded population of NK cells of claim 10 or 11 or the composition of claim 12.

16. The method according to any one of claims 13-15 further comprising administering to the subject at least one cancer therapeutic agent in combination with the effective amount of the composition or expanded NK cell population.
17. A method of modulating T cell repertoire during or after stem cell transplant comprising administering to a subject in need thereof an effective amount of the expanded population of NK cells of claim 10 or 11 or the composition of claim 12.
18. A method of preventing, inhibiting, reducing, or mitigating acute or chronic graft-vs-host disease comprising administering to a subject in need thereof an effective amount of the expanded population of NK cells of claim 10 or 11 or the composition of claim 12.
19. A method of preventing, inhibiting, reducing, or mitigating viral reactivation comprising administering to a subject in need thereof an effective amount of the expanded population of NK cells of claim 10 or 11 or the composition of claim 12.
20. A method of preventing, inhibiting, reducing, or mitigating opportunistic infections comprising administering to a subject in need thereof an effective amount of the expanded populations of NK cells of claim 10 or 11 or the composition of claim 12.
21. The expanded population of NK cells of claim 10 or 11, wherein the expanded NK cells exhibit increased secretion of anti-tumor cytokines compared with non-expanded NK cells or exhibit increased expression of NKG2D, NKp46 and CD16 compared with non-expanded NK cells.
22. A method of increasing NK cell cytotoxicity, comprising exposing an initial population of NK cells in vitro to an NK cell expanding composition, the composition comprising at least one feeder cell or engineered particle comprising at least two NK cell effector agents, wherein one of the at least two NK cell effector agents is IL-21, and an Fc domain bound to an external surface of the feeder cell or engineered particle.

23. The method of claim 22, wherein the NK cell expanding composition comprises at least one feeder cell having a membrane bound Fc domain.
24. The method of claim 22, wherein the NK cell expanding composition comprises at least an engineered particle selected from a PM particle having a membrane bound Fc domain and an exosome having a membrane bound Fc domain.
25. The method of claim 22, further comprising obtaining a population of expanded NK cells having increased cytotoxicity compared to the initial population of NK cells.