

~~That which is claimed is:~~ **Claims**

1. A nanoparticle comprising:
at least ~~one~~ two first targeting agents ~~that binds~~ bind ~~a~~ at least one first target on a natural killer (NK) cell surface; and
at least one second targeting agent that binds a second target on a cancer cell surface, wherein the second targeting agent is different from the first targeting agent.
- ~~2. The nanoparticle of claim 1, comprising at least two first targeting agents.~~
- ~~3~~2. The nanoparticle of claim ~~2~~1, wherein the at least two first targeting agents are two different first targeting agents that bind at least two different first targets on the NK cell surface.
- ~~4~~3. The nanoparticle of any one of claims 1-~~3~~2, wherein the first target on the NK cell surface is selected from the group consisting of CD16, 4-1BB, NKG2D, TRAIL, NKG2C, CD137, OX40, CD27, KIRs, NKG2a, dnam-1, 2b4, NKp30a, NKp30b, NKp30c, antibody Fc component, and any combination thereof;
- ~~5. The nanoparticle of claim 4, wherein, optionally, the first target on the NK cell surface is CD16 and/or 4-1BB.~~
- ~~6~~4. The nanoparticle of any one of claims 1-~~5~~3, wherein the cancer cell is a cell from ~~aan~~ adenocarcinoma, thymoma, sarcoma, brain cancer, head and neck cancer, esophageal cancer, gastric cancer, lung cancer, bladder cancer, kidney cancer, liver cancer, pancreatic cancer, uterine cancer, ovarian cancer, cervical cancer, anal cancer, melanoma, prostate cancer, breast cancer, blood cell cancer, colorectal cancer, or any combination thereof.
- ~~7~~5. The nanoparticle of any one of claims 1-~~6~~4, wherein the second target on the cancer cell surface is selected from the group consisting of EGFR, PSMA, Nectin-4, mucin, HER-2, CD30, CD22, and any combination thereof;
- ~~8. The nanoparticle of claim 7, wherein, optionally, the second target on the cancer cell surface is EGFR.~~

96. The nanoparticle of any one of claims 1-85, wherein the first targeting agent and/or the second targeting agent is an antibody or active fragment thereof;

~~10. The nanoparticle of claim 9, wherein, optionally, the antibody or active fragment thereof is selected from the group consisting of a monoclonal antibody, a Fab fragment, a Fab'-SH fragment, a FV fragment, a scFV fragment, a (Fab')₂ fragment, an Fc-fusion protein, and any combination thereof.~~

~~117. The nanoparticle of any one of claims 1-106, further comprising a therapeutic agent;~~

~~12. The nanoparticle of claim 11, wherein, optionally, the therapeutic agent is a chemotherapeutic agent selected from the group consisting of epirubicin (EPI), doxorubicin, cisplatin, oxaliplatin, carboplatin, daunorubicin, taxol, docetaxel, gemcitabine, 5-fluorouracil, mitomycin, cytarabine, cytoxan, and any combination thereof;~~

~~13. The nanoparticle of claim 12, wherein, further optionally, the chemotherapeutic agent is epirubicin (EPI).~~

148. A composition comprising the nanoparticle of any one of claims 1-137 and a pharmaceutically acceptable carrier.

~~15. A method of activating an NK cell, comprising contacting the NK cell with the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 under conditions whereby the first targeting agent binds the first target on the NK cell surface.~~

~~16. A method of inducing an NK cell immune response, comprising contacting the NK cell with the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 under conditions whereby the first targeting agent binds the first target on the NK cell surface.~~

~~17. A method of inducing cytotoxicity in a cancer cell, comprising contacting the cancer cell with the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 under conditions whereby the second targeting agent binds the second target on the surface of the cancer cell.~~

18. — The method of claim 17, wherein the nanoparticle or composition further comprises a therapeutic agent.

19. — A method of delivering a therapeutic agent to a cancer cell, comprising contacting the cancer cell with the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 comprising a therapeutic agent, under conditions whereby the second targeting agent binds the second target on the surface of the cancer cell, thereby delivering the therapeutic agent to the cancer cell.

20. — A method of inducing an NK cell immune response in a subject in need thereof, comprising administering to the subject an effective amount of the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 under conditions whereby the first targeting agent binds the first target on the surface of the NK cell.

21. — The method of claim 20, wherein the nanoparticle and/or composition comprises at least two first targeting agents and wherein the NK cell that the at least two first targeting agents bind is the same NK cell.

22. — A method of activating NK cells in a subject in need thereof, comprising administering to the subject an effective amount of the nanoparticle of any one of claims 1-13 and/or the composition of claim 14 under conditions whereby the first targeting agent binds the first target on the surface of the NK cell.

23. — The method of claim 22, wherein the nanoparticle and/or composition comprises at least two first targeting agents and wherein the NK cell that the at least two first targeting agents bind is the same NK cell.

24. — The method of any one of claims 20-23, wherein the subject has been diagnosed with cancer.

25. — A method of treating cancer in a subject in need thereof, comprising administering to the subject an effective amount of the nanoparticle of any one of claims 1-13 and/or the

~~composition of claim 14 under conditions whereby the second targeting agent binds the second target on the surface of the cancer cell.~~

269. A nanoparticle of any one of claims 1-7 and/or a composition of claim 8 for use in a method of treating cancer in a subject in need thereof, comprising administering to the subject an effective amount of the nanoparticle of any one of claims 1-13-7 and/or the composition of claim 14-8 under conditions whereby the at least two first targeting agents binds the at least first target on the surface of the NK cell and whereby the at least one second agent binds the second target on the surface of the cancer cell.

~~27. A method of delivering a therapeutic agent to a cancer cell of a cancer in a subject in need thereof, comprising administering to the subject an effective amount of the nanoparticle of any one of claims 1-13 or the composition of claim 14 comprising a therapeutic agent, under conditions whereby the second targeting agent binds the second target on the surface of the cancer cell, thereby delivering the therapeutic to the cancer cell in the subject.~~

2810. The nanoparticle and/or composition for use method of any one of claims 24-27-claim 9, wherein the cancer is selected from the group consisting of glioblastoma, head and neck cancer, esophageal cancer, gastric cancer, lung cancer, bladder cancer, renal cell carcinoma, hepatocellular carcinoma, pancreatic cancer, cervical cancer, anal cancer, melanoma, prostate cancer, breast cancer, non-Hodgkin's lymphoma or colorectal cancer and any combination thereof.

2911. The nanoparticle and/or composition for use method of any of claims 20-289-10, wherein the nanoparticle or composition is administered via a route selected from the group consisting of intravenous, intramuscular, subcutaneous, topical, oral, transdermal, intraperitoneal, intrathecal, intraventricular, intravitreal, intraocular, intraorbital, intranasal, by implantation, by inhalation, by intratumoral, and any combination thereof.

3012. The nanoparticle and/or composition for use method of any of claims 20-299-11, further comprising the step of administering to the subject an effective amount of a therapeutic agent and/or radiation therapy.

~~31~~13. The nanoparticle and/or composition for use ~~method~~ of claim ~~30~~12, wherein the therapeutic agent is a chemotherapeutic agent selected from the group consisting of epirubicin (EPI), doxorubicin, cisplatin, oxaliplatin, carboplatin, daunorubicin, taxol, docetaxel, gemcitabine, 5-fluorouracil, mitomycin, cytarabine, cytoxan, and any combination thereof;

~~32~~. — ~~The method of claim 31~~, wherein, optionally, the chemotherapeutic agent is epirubicin (EPI).

~~33~~14. The nanoparticle and/or composition for use ~~method~~ of any of claims ~~20-32~~9-13, wherein the subject is a mammal;

~~34~~. — ~~The method of claim 33~~, wherein, optionally, the mammal is a human.

~~35~~15. A kit comprising the nanoparticle of any of claims ~~1-13~~7 and/or the composition of claim ~~14-8~~ and instructions for use.

~~36~~16. ~~Use of the~~The nanoparticle of any of claims ~~1-13~~7 and/or the composition of claim ~~14-8 for use~~ in activating NK cells.

~~37~~17. ~~Use of the~~The nanoparticle of any of claims ~~1-13~~7 and/or the composition of claim ~~14-8 for use~~ in inducing cytotoxicity in a cancer cell.

~~38~~18. ~~Use of the~~The nanoparticle of any of claims ~~1-13~~7 and/or the composition of claim ~~14-8 for use~~ in delivering a therapeutic agent to a cancer cell.

~~39~~19. ~~Use of the~~The nanoparticle of any of claims ~~1-13~~7 and/or the composition of claim ~~14-8 for use~~ in treating cancer.

~~4020. Preparation of a medicament for use comprising~~ Use of the nanoparticle of any of
claims ~~1-13~~ 1-7 and/or the composition of claim ~~14~~ 8 in the manufacture of a medicament for
treatment of cancer.