

CLAIMS

What is claimed is:

1. A composition comprising natural killer (NK) cells, said NK cells comprising one or more exogenously provided interleukins (IL), wherein the IL is not IL-15, and wherein the NK cell comprises one or more engineered receptors.
2. The composition of claim 1, wherein the IL is selected from the group consisting of IL-12, IL-21, IL-2, IL-18, IL-7, the p35 and p40 subunits of IL-12 artificially linked together with a linker, and a combination thereof.
3. The composition of claim 1 or 2, wherein the IL is IL-12, IL-21, or both.
4. The composition of any one of claims 1-3, wherein said IL is secreted, tethered, or membrane bound in the cell.
5. The composition of any one of claims 1-4, wherein exogenously provided is further defined as being expressed from a vector in the cells and/or wherein the NK cells are cultured in the presence of one or more IL.
6. The composition of any one of claims 1-5, wherein the engineered receptor is an engineered antigen receptor.
7. The composition of claim 6, wherein the engineered antigen receptor is a chimeric antigen receptor (CAR) or a T cell receptor (TCR).
8. The composition of claim 6 or 7, wherein the antigen is a cancer antigen.
9. The composition of any one of claims 6-8, wherein the antigen is a solid tumor antigen.
10. The composition of any one of claims 6-9, wherein the antigen is selected from the group consisting of 5T4, 8H9, $\alpha_v\beta_6$ integrin, BCMA, B7-H3, B7-H6, CAIX, CA9, CD5, CD19, CD20, CD22, CD30, CD33, CD38, CD44, CD44v6, CD44v7/8, CD70, CD123, CD138, CD171, CEA, CSPG4, CS1, CLL1, CD99, DLL3, EGFR, EGFR family including ErbB2 (HER2), EGFRvIII, EGP2, EGP40, , ERBB3, ERBB4, ErbB3/4, EPCAM, EphA2, EpCAM, FAP, FBP, fetal AchR, FR α , GD2, GD3, Glypican-3 (GPC3), HLA-A1+MAGE1, HLA-A1+NY-ESO-1, IL-11R α , IL-

13R α 2, Lambda, Lewis-Y, L1CAM, Kappa, KDR, MCSP, Mesothelin, Muc1, Muc16, NCAM, NKG2D Ligands, NY-ESO-1, PRAME, PSC1, PSCA, PSMA, ROR1, SP17, Survivin, TAG72, TEMs, HMW-MAA, and VEGFR2.

11. The composition of claim 6, wherein the engineered receptor is a cytokine receptor, chemokine receptor, or homing receptor.

12. The composition of any one of claims 1-11, wherein the NK cell comprises a suicide gene.

13. The composition of any one of claims 1-12, wherein the cell is reduced or inhibited in expression of one or more of endogenous genes selected from the group consisting of TDAG8, NKG2A, SIGLEC-7, LAG3, TIM3, CISH, FOXO1, TGFBR2, TIGIT, CD96, ADORA2, NR3C1, PD1, PDL-1, PDL-2, CD47, SIRPA, SHIP1, ADAM17, RPS6, 4EBP1, CD25, CD40, IL21R, ICAM1, CD95, CD80, CD86, IL10R, CD5, CD7, and a combination thereof.

14. A population of cells comprising the composition of any one of claims 1-13, comprised in a suitable medium.

15. A method of treating cancer in an individual, comprising the step of administering a therapeutically effective amount of the compositions of any one of claims 1-13 to the individual.

16. The method of claim 15, wherein cancer cells in the individual have increased expression of NK ligands.

17. The method of claim 15 or 16, wherein the cancer cells in the individual have increased expression of MICA/B, ULBP1, ULBP2/5, ULBP3, B7-H6, CD112, CD155, HLA-ABC, HLA-DR, HLA-3, or a combination thereof.

18. The method of any one of claims 15-17, wherein the cancer is a solid tumor or is not a solid tumor.

19. The method of any one of claims 15-18, wherein the cancer is of the lung, brain, breast, blood, skin, pancreas, liver, colon, head and neck, kidney, thyroid, stomach, spleen, gallbladder, bone, ovary, testes, endometrium, prostate, rectum, anus, cervix, or is hematological.

20. The method of any one of claims 15-19, wherein the cancer is glioblastoma.

21. The method of any one of claims 15-20, wherein the individual is a mammal.
22. The method of any one of claims 15-21, wherein the individual is a human, dog, cat, horse, cow, sheep, pig, or rodent.
23. The method of any one of claims 15-22, wherein the individual is administered one or more additional cancer therapies.
24. The method of claim 23, wherein the additional cancer therapy is surgery, radiation, chemotherapy, hormone therapy, immunotherapy, or a combination thereof.
25. The method of any one of claims 15-24, further comprising the step of diagnosing cancer in the individual.
26. The method of any one of claims 15-25, further comprising the step of generating the cells.
27. The method of any one of claims 15-26, wherein the cells are autologous with respect to the individual.
28. The method of any one of claims 15-26, wherein the cells are allogeneic with respect to the individual.
29. The method of any one of claims 15-28, wherein the population of cells are administered to the individual intracranially, by injection, intravenously, intraarterially, intraperitoneally, intratracheally, intratumorally, intramuscularly, endoscopically, intralesionally, intracranially, percutaneously, subcutaneously, regionally, by perfusion, in a tumor microenvironment, or a combination thereof.