CLAIMS

1. A nanoparticle comprising:

a targeting ligand that binds to a professional phagocyte; and

a nucleic acid that encodes a protein molecule having at least a first binding domain and a second binding domain,

wherein the first binding domain is specific to a cell surface protein expressed by an immune cell, and

wherein the second binding domain is specific to a cell surface protein expressed by a cancer cell.

2. The nanoparticle of claim 1, wherein the targeting ligand binds to a cell surface protein expressed by a monocyte, a macrophage, or both.
3. The nanoparticle of claim 1, wherein the nucleic acid comprises ribonucleic acid (RNA).
4. The nanoparticle of claim 1, wherein the first binding domain is specific to a cell surface protein of a lymphocyte.
5. The nanoparticle of claim 1, wherein the first binding domain is specific to a cell surface protein of a T-cell selected from the group consisting of a CD8+ T cell, CD4+ T cell, a gamma delta T cell, and an NK T-cell.
6. The nanoparticle of claim 1, wherein the protein molecule is a bi-specific T-cell engager.
7. The nanoparticle of claim 1, wherein the second binding domain is specific to an antigen expressed by the cancer cell.
8. The nanoparticle of claim 1, further comprising a second nucleic acid that encodes one or more interferon regulatory factors (IRFs).
9. The nanoparticle of claim 1, further comprising a tumor cell proliferation inhibitor or a nucleic acid encoding a tumor cell proliferation inhibitor.
10. The nanoparticle of claim 1, wherein the nanoparticle is a liposome, a liposomal nanoparticle, a lipid nanoparticle, or a solid lipid nanoparticle.
11. A composition comprising:

at least one nanoparticle of any one of claim 1 to claim 10.

12. A composition for use in treating cancer in a human subject, the composition comprising:

a first plurality of nanoparticles comprising at least one nanoparticle of any one of claim 1 to claim 10,

wherein the first plurality of nanoparticles stimulates or enhances an immune response in the human subject, thereby treating cancer.

13. Use of a composition comprising the nanoparticle of any one of claims 1-10 in the preparation

of a medicament for treating cancer in a human subject.

14. The use of claim 13, further comprising:

a composition comprising a second plurality of nanoparticles to be administered to the human subject, wherein each of the second plurality of nanoparticles comprises

a targeting ligand that binds to a monocyte, a macrophage, or both, and

one or more of (a) an mRNA encoding one or more interferon regulatory factors (IRFs), and (b) an mRNA encoding IKKβ.

15. The use of claim 14, wherein at least a subset of the first or second plurality of nanoparticles further comprise an mRNA encoding a tumor cell proliferation inhibitor.

16. The use of any of claim 14, further comprising:

a composition comprising a third plurality of nanoparticles to be administered to the human subject, wherein each of the third plurality of nanoparticles comprises

a targeting ligand that binds to a monocyte, a macrophage, or both, and

an mRNA encoding a tumor cell proliferation inhibitor.

17. A modified professional phagocyte comprising:

a nanoparticle loaded with a nucleic acid encoding a protein molecule having at least a first binding domain specific to a cell surface protein expressed by an immune cell and a second binding domain specific for a cell surface protein expressed by cancer cell,

wherein the nanoparticle is adhered to the surface of the phagocyte or has been internalized by the phagocyte.

18. The modified professional phagocyte of claim 17, further comprising at least one of

a second nanoparticle loaded with one or more of (a) a nucleic acid encoding one or more interferon regulatory factors (IRFs), (b) a nucleic acid encoding IKKβ, or (c) a nucleic acid encoding a tumor cell proliferation inhibitor; and

a third nanoparticle loaded with a nucleic acid encoding a tumor cell proliferation inhibitor, wherein each of the second and third nanoparticles is adhered to the surface of the phagocyte or has been internalized by the phagocyte.

19. A nanoparticle comprising a positively-charged polymer core and a neutral or negatively-charged coating around the polymer core wherein the positively-charged polymer core encapsulates nucleotides encoding at least one binding domain that binds an immune cell activating epitope and/or at least one binding domain that binds a cancer antigen.

20. A system comprising:

nanoparticles

wherein at least a subset of the nanoparticles comprise nucleotides encoding one

or more interferon regulatory factors (IRFs) and

wherein at least a subset of the nanoparticles comprise nucleotides encoding a protein molecule having at least two binding domains

wherein one binding domain binds an antigen expressed by a cancer cell at a tumor site and

wherein one binding domain binds an immune cell activating epitope.

21. A monocyte or macrophage genetically modified to express the nucleotides of a system of claim 20.
22. Use of the system of claim 20 in the preparation of a medicament for modulating the macrophage activation state at a tumor site within a subject, comprising recruiting immune cells to the tumor site, and activating the recruited immune cells comprising:

the system to be administered to the subject, thereby modulating the macrophage activation state at the tumor site within the subject, recruiting immune cells to the tumor site, and activating the recruited immune cells.

23. The use of claim 22, wherein the medicament is for treating cancer in a human subject.