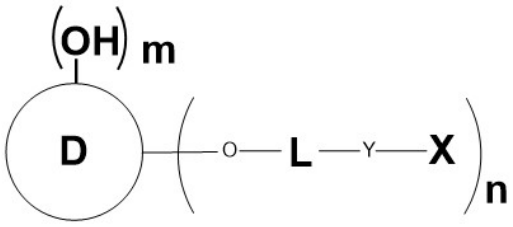
We claim:

1. A composition comprising a dendrimer complexed or covalently conjugated with one or more immunomodulatory agents in an amount effective to suppress or inhibit one or more immunosuppressive cells associated with a tumor in a subject in need thereof, wherein the dendrimer complexed or covalently conjugated with one or more immunomodulatory agents comprises a compound of Formula (I):



Formula (I),

wherein:

D is a generation 2 to generation 10 poly(amidoamine) (PAMAM) dendrimer;

L is one or more linking moieties or spacers, wherein L comprises a polyethylene glycol (PEG) and a triazole linker;

X is an immunomodulatory agent or analog thereof, wherein X is a CSF1R tyrosine kinase inhibitor, VEGFR tyrosine kinase inhibitor, EGFR tyrosine kinase inhibitor, or a derivative, an analogue or a prodrug thereof;

n is an integer from 1 to 100;

m is an integer from 16 to 4096;

Y is selected from secondary amides, tertiary amides, sulfonamide, secondary carbamates, tertiary carbamates, carbonate, ureas, carbinols, disulfide groups, hydrazones, hydrazides, and ethers.

2. The composition of claim 1, wherein:

Y is -O-, -CONH-, -CONR-, -$S(O)_2$-NR-, -OCONH-, -NHCOO-, -OCONR-, -NRCOO-, -O-C(O)-O-, -NHCONH-, -NRCONH-, -NHCONR-, -NRCONR-, -CHOH-, -CROH-, or -S-S-; and

R is an alkyl group, an aryl group, or a heterocyclic group.

3. The composition of claim 1 or 2, wherein n is 5-15, and m is 49-59.

4. The composition of any one of claims 1-3, wherein n+m=64.

5. The composition of any one of claims 1-4, wherein D is a generation 4, generation 5, or generation 6 PAMAM dendrimer.

6. The composition of any one of claims 1-5, wherein X is a CSF1R tyrosine kinase inhibitor.

7. The composition of claim 6, wherein the CSF1R tyrosine kinase inhibitor is selected from the group consisting of PLX3397, PLX108-01, ARRY-382, PLX7486, BLZ945, JNJ-40346527, and GW 2580.

8. The composition of any one of claims 1-5, wherein X is a VEGFR tyrosine kinase inhibitor.

9. The composition of claim 8, wherein the VEGFR tyrosine kinase inhibitor is selected from the group consisting of sunitinib, sorafenib, pazopanib, vandetanib, axitinib, cediranib, vatalanib, dasatinib, nintedanib, and motesanib.

10. The composition of claim 8, wherein the VEGFR tyrosine kinase inhibitor is sunitinib, or a derivative of didesethyl sunitinib.

11. The composition of any one of claims 1-10, wherein the one or more immunosuppressive cells are myeloid-derived suppressor cells and/or tumor-associated macrophages (M2 macrophages).

12. A pharmaceutical composition comprising an effective amount of the composition of any one of claims 1-11.

13. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein an effective amount of the pharmaceutical composition is to be administered to the subject.

14. The use of claim 13, wherein the cancer is breast cancer, ovarian cancer, uterine cancer, prostate cancer, testicular germ cell tumor, brain cancer, gastric cancer, esophagus cancer, lung cancer, liver cancer, renal cell cancer, or colon cancer.

15. The use of claim 13 or 14, wherein the effective amount is effective to reduce tumor size.

16. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for reducing or inhibiting one or more immunosuppressive cells at a site of tumor in a subject identified as having cancer, wherein an effective amount of the pharmaceutical composition is to be administered to the subject.

17. The use of claim 16, wherein the immunosuppressive cells are myeloid-derived suppressor cells and/or tumor-associated macrophages (M2 macrophages).

18. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for enhancing tumour-specific cytotoxic T cell responses in a subject identified as having cancer, wherein an effective amount of the pharmaceutical composition is to be administered to the subject.

19. The use of any one of claims 13-18, wherein one or more immune checkpoint modulators selected from the group consisting of PD-1 antagonists, PD-1 ligand antagonists, and CTLA4 antagonists is to be further administered to the subject.

20. The use of any one of claims 13-18, wherein one or more additional active agents selected from the group consisting of a chemotherapeutic agent, an anti-infective agent, and combinations thereof is to be further administered to the subject.

21. The use of any one of claims 13-18, wherein adoptive T cell therapy, and/or a cancer vaccine is to be further administered to the subject.

22. The use of any one of claims 13-18, wherein surgery or radiation therapy is to be further administered to the subject.

23. The composition of any of claims 1-11 for use as a medicament.