CLAIMS

We claim:

1. A composition comprising hydroxyl-terminated dendrimers conjugated to one or more radionuclides or one or more magnetic resonance imaging (MRI) contrast agents through ether linkages, optionally via one or more linking moieties.

2. The composition of claim 1, wherein the dendrimers are polyamidoamine (PAMAM) dendrimers, polypropylamine (POPAM) dendrimers, polyethylenimine dendrimers, polylysine dendrimers, polyester dendrimers, iptycene dendrimers, aliphatic poly(ether) dendrimers, or aromatic polyether dendrimers.

3. The composition of claim 2, wherein the dendrimers are generation 4, generation 5, generation 6, generation 7, or generation 8 PAMAM dendrimers.

4. The composition of any one of claims 1-3, wherein the one or more radionuclides are selected from the group consisting of ^{18}F, ^{51}Mn, ^{52}Fe, ^{60}Cu, ^{68}Ga, ^{72}As, ^{94m}Tc, or ^{110}In, ^{18}F, ^{124}I, ^{125}I, ^{131}I, ^{123}I, ^{77}Br, ^{76}Br, ^{99m}Tc, ^{51}Cr, ^{67}Ga, ^{68}Ga, ^{47}Sc, ^{51}Cr, ^{167}Tm, ^{141}Ce, ^{111}In , ^{168}Yb, ^{175}Yb, ^{140}La, ^{90}Y, ^{88}Y, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{166}Dy, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, ^{188}Re, ^{203}Pb, ^{211}Bi, ^{212}Bi, ^{213}Bi, ^{214}Bi, ^{105}Rh, ^{109}Pd, ^{117m}Sn, ^{149}Pm, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{198}Au, ~~and~~ ^{199}Au, and ~~or~~ ^{89}Zr.

5. The composition of any one of claims 1-4, wherein the one or more radionuclides are ^{18}F, ^{89}Zr, ^{90}Y, or ^{177}Lu.

6. The composition of any one of claims 1-3, wherein the one or more MRI contrast agents are selected from a group consisting of Gd, Mn, $BaSO_4$, iron oxides, and iron platinum.

7. The composition of any one of claims 1-3 and 6, wherein the MRI contrast agent is Gd.

8. The composition of any one of claims 1-7 in an amount effective to selectively accumulate within reactive microglia and/or macrophages at sites of inflammation or in reactive immune cells in tumors.

9. The composition of any one of claims 1-7, further comprising one or more additional active agents.

10. A composition comprising a compound that comprises a dendrimer conjugated to a radionuclide or an MRI contrast agent through an ester, ether, or amide linkage, wherein the dendrimer comprises a high density of surface hydroxyl groups.

11. The composition of claim 10, wherein the radionuclide or the MRI contrast agent is conjugated to the ester, ether, or amide linkage through a spacer.

12. The composition of claim 11, wherein the spacer comprises alkyl groups, heteroalkyl groups, or alkylaryl groups.

13. The composition of claim 11 or 12, wherein the spacer comprises a peptide.

14. The composition of any one of claims 11-13, wherein the spacer comprises polyethylene glycol.

15. The composition of any one of claims 10-14, wherein conjugation of the radionuclide or the MRI contrast agent occurs on less than 50% of total available surface functional groups of the dendrimer prior to the conjugation.

16. The composition of any one of claims 10-15, wherein conjugation of the radionuclide or the MRI contrast agent occurs on less than 5%, less than 10%, less than 20%, less than 30%, or less than 40% of total available surface functional groups of the dendrimer prior to the conjugation.

17. The composition of any one of claims 10-16, wherein the radionuclide is selected from the group consisting of ^{18}F, ^{51}Mn, ^{52}Fe, ^{60}Cu, ^{68}Ga, ^{72}As, ^{94m}Tc, ^{110}In, ^{18}F, ^{124}I, ^{125}I, ^{131}I, ^{123}I, ^{77}Br, ^{76}Br, ^{99m}Tc, ^{51}Cr, ^{67}Ga, ^{68}Ga, ^{47}Sc, ^{51}Cr, ^{167}Tm, ^{141}Ce, ^{111}In, ^{168}Yb, ^{175}Yb, ^{140}La, ^{90}Y, ^{88}Y, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{166}Dy, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, ^{188}Re, ^{203}Pb, ^{211}Bi, ^{212}Bi, ^{213}Bi, ^{214}Bi, ^{105}Rh, ^{109}Pd, ^{117m}Sn, ^{149}Pm, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{198}Au, ^{199}Au, and ^{89}Zr.

18. The composition of claim 17, wherein the radionuclide is ^{18}F, ^{89}Zr, ^{90}Y, or ^{177}Lu.

19. The composition of any one of claims 10-16, wherein the MRI contrast agent is selected from the group consisting of Gd, Mn, $BaSO_4$, iron oxides, and iron platinum.

20. The composition of claim 19, wherein the MRI contrast agent is Gd.

21. The composition of any one of claims 10-20, wherein the dendrimer is selected from the group consisting of polyamidoamine (PAMAM) dendrimers, polypropylamine (POPAM) dendrimers, polyethylenimine dendrimers, polylysine dendrimers, polyester dendrimers, iptycene dendrimers, aliphatic poly(ether) dendrimers, and aromatic polyether dendrimers.

22. The composition of any one of claims 10-21, wherein the zeta potential of the compound is between -25 mV and 25 mV.

23. The composition of any one of claims 10-22, wherein the zeta potential of the compound is between -20 mV and 20 mV, between -10 mV and 10 mV, between -10 mV and 5 mV, between -5 mV and 5 mV, or between -2 mV and 2 mV.

24. The composition of any one of claims 10-23, wherein the surface charge of the compound is neutral or near-neutral.

25. The composition of any one of claims 10-24, wherein the dendrimer is conjugated to the radionuclide or the MRI contrast agent through an ether or amide linkage.

26. The composition of any one of claims 10-25, wherein the dendrimer is conjugated to the radionuclide or the MRI contrast agent through an ether linkage.

27. A pharmaceutical composition comprising the composition of any one of claims 1-26 and a pharmaceutically acceptable excipient.

28. The pharmaceutical composition of claim 27, formulated for intraperitoneal, intravenous, intrathecal, intratumoral, or oral administration.

29. A method for detecting or imaging one or more inflammatory and/or cancer cells in a subject in need thereof, wherein an effective amount of a composition is to be administered ~~the method comprising administering~~ to the subject, ~~an effective amount of a~~ the composition comprising a compound that comprises a dendrimer conjugated to a radionuclide or an MRI contrast agent through an ester, ether, or amide linkage, wherein the dendrimer comprises a high density of surface hydroxyl groups.

30. The method of claim 29, wherein the composition is to be administered systemically to the subject.

31. The method of claim 29 or claim 30, wherein the composition is to be administered via intraperitoneal, intravenous, intrathecal, intratumoral, or oral route.

32. The method of any one of claims 29-31, wherein the composition is to be administered in an amount effective to detect, diagnose or monitor one or more inflammatory sites or cancer in the subject.

33. The method of any one of claims 29-32, wherein the one or more inflammatory sites in the subject are associated with one or more inflammatory diseases, or associated with sepsis or septic shock, or caused by any mechanism of macrophage activation including macrophage activation syndrome.

34. The method of any one of claims 29-32, wherein the one or more inflammatory sites in the subject are associated with one or more autoimmune diseases or disorders.

35. The method of claim 34, wherein the one or more autoimmune diseases or disorders are selected from the group consisting of rheumatoid arthritis, psoriasis, psoriatic arthritis, multiple sclerosis, Sjögren syndrome, Myasthenia gravis, Graves disease, Addison disease, Celiac disease, Hashimoto thyroiditis, Pernicious anemia, Guillain-Barre syndrome, Chronic inflammatory demyelinating polyneuropathy, vasculitis, systemic lupus erythematosus (SLE), type 1 diabetes, inflammatory bowel disease, and thyroid diseases.

36. The method of any one of claims 29-32, wherein the one or more inflammatory sites in the subject include one or more sites of neuroinflammation in the central nervous system.

37. The method of claim 36, wherein the one or more sites of neuroinflammation in the central nervous system in the subject are associated with Alzheimer's disease.

38. The method of any one of claims 29-32, wherein the one or more inflammatory sites in the subject are associated with amyotrophic lateral sclerosis (ALS).

39. The method of any one of claims 29-32, wherein the subject has cancer.

40. The method of claim 39, wherein the cancer is solid tumor of any type or brain metastases.

41. The method of any one of claims 29-40, wherein the method further comprises the step of imaging the subject with a molecular imaging device to detect the dendrimers conjugated to one or more radionuclides in the subject, wherein detection of the dendrimers conjugated to one or more radionuclides indicates presence of inflammation or cancer cells.

42. The method of claim 41, wherein the molecular imaging device comprises a gamma camera for positron emission tomography (PET) scanning or a scanner for magnetic resonance imaging.

43. A method for detecting or imaging one or more inflammatory and/or cancer cells in a subject in need thereof, wherein ~~the method comprising administering to the subject~~ an effective amount of the composition of any one of claims 1-28 is to be administered to the subject.

44. Use ~~A method for treating cancer comprising administering to a subject in need thereof an effective amount~~ of the composition of any one of claims 1-28 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the composition is to be administered to the subject.

45. ~~A method for treating cancer comprising administering to a subject in need thereof an effective amount~~Use of a composition comprising a compound that comprises a dendrimer conjugated to a radionuclide or an MRI contrast agent through an ester, ether, or amide linkage, in the manufacture of a medicament for treating cancer in a subject in need thereof,

wherein the composition is to be administered to the subject in an effective amount to treat the cancer,

wherein the dendrimer comprises a high density of surface hydroxyl groups.

46. The ~~method~~ use of claim 45, ~~wherein the~~ wherein the composition is to be administered systemically to the subject.

47. The use ~~method~~ of claim 45 or claim 46, wherein the composition is to be administered via intraperitoneal, intravenous, intrathecal, intratumoral or oral route.

48. The use ~~method~~ of any one of claims 45-47, 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 ~~and~~ colon cancer.

49. The use ~~method~~ of any one of claims 45-48, wherein the effective amount is effective to reduce tumor size.

50. A method of making hydroxyl dendrimers covalently conjugated via ether linkages to one or more positron emission tomography (PET) imaging agents or one or more magnetic resonance imaging (MRI) contrast agents, the method comprising etherification of one or more surface groups of the dendrimers prior to conjugation of the one or more surface groups of the dendrimers to one or more PET imaging agents, optionally via one or more spacers, and wherein the conjugation is via an ether linkage.

51. The method of claim 50, wherein the PET imaging agent or the MRI contrast agent comprises a chelator selected from the group consisting of p-SCN-Bn-Deferoxamine, diethylene triamine pent-acetic acid (DTPA), 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA), diamine dithiols, activated mercaptoacetyl-glycyl-glycyl-glycine (MAG3), and hydrazidonicotinamide (HYNIC).

52. The method of claim 50 or claim 51, wherein the PET imaging agent comprises radionuclides selected from the group consisting of ^{64}Cu, ^{89}Zr, ^{90}Y, ^{105}Rh, $^{-111}In^{-}$, ^{117m}Sn, ^{149}Pm, ^{153}Sm, ^{161}Tb, ^{166}Tb, ^{166}Dy, ^{166}Ho, ^{175}Yb, ^{177}Lu, ^{225}Ac, $^{186/188}Re$, and ^{199}Au.

53. The method of claim 50 or claim 51, wherein the MRI contrast agent comprises metals selected from the group consisting of Gd, Mn, $BaSO_4$, iron oxides, and iron platinum.

54. The method of any one of claims 50-53, wherein the dendrimer is further complexed and/or conjugated to one or more therapeutic, prophylactic, and/or diagnostic agents.

55. ~~A method for treating a neurodegenerative disorder comprising administering to a subject in need thereof an effective amount~~Use of a composition comprising a compound that comprises a dendrimer conjugated to a radionuclide or an MRI contrast agent through an ester, ether, or amide linkage, in the manufacture of a medicament for treating a neurodegenerative disorder in a subject in need thereof,

wherein the composition is to be administered to the subject in an effective amount to treat the neurodegenerative disorder,

wherein the dendrimer comprises a high density of surface hydroxyl groups.

56. The ~~method~~ use of claim 55, wherein the neurodegenerative disorder is Alzheimer's disease.

57. The ~~method~~ use of claim 55, wherein the neurodegenerative disorder is ALS.