(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 October 2023 (26.10.2023)

WIPO | PCT

(10) International Publication Number
WO 2023/201435 A8

(51) International Patent Classification:
C07K 7/56 (2006.01) *A61P 35/00* (2006.01)
A61K 47/62 (2017.01) *C07K 1/13* (2006.01)
A61K 51/08 (2006.01) *C07K 7/02* (2006.01)

(21) International Application Number:
PCT/CA2023/050538

(22) International Filing Date:
20 April 2023 (20.04.2023)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/332,885 20 April 2022 (20.04.2022) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE*

(48) Date of publication of this corrected version:
28 December 2023 (28.12.2023)

(15) Information about Correction:
see Notice of 28 December 2023 (28.12.2023)

(54) Title: CXCR4-TARGETING COMPOUNDS, AND METHODS OF MAKING AND USING THE SAME

(57) Abstract: The present disclosure relates to peptidic compounds of Formula A, A-II, A-III, A-III, A- IV, B, or C, or salt or solvate thereof, compositions thereof, and methods of use thereof. The compounds of the present disclosure are useful for targeting CXCR4 for purposes such as imaging and/or therapeutics.

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CXCR4-TARGETING COMPOUNDS, AND METHODS OF MAKING AND USING THE SAME

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 63/332,885, filed April 20, 2022, the disclosure of which is hereby incorporated by reference in its entirety.

FIELD OF INVENTION

[0002] The present invention relates to novel peptidic compounds, particularly compounds that target CXCR4 for purposes such as imaging and/or therapeutics.

BACKGROUND OF THE INVENTION

[0003] C-X-C chemokine receptor type 4 (CXCR4) is a G protein-coupled transmembrane receptor that is expressed in hematological and immune tissues and systems.[1,2] CXCR4 has only one chemokine as a substrate named stromal-derived-factor-1 (SDF-1), also known as CXCL12.[3] CXCR4 is aberrantly expressed in a number of important pathologies that involve inflammation and immune cell trafficking, including athersclerosis,[4] systemic erythematous lupus[5,6], cancer and others. Importantly, CXCR4 has been found to play key roles in tumourigenesis, chemoresistance and metastasis and its expression has been detected in more than twenty different subtypes of cancers with an accompanying negative prognosis.[7–12] As such, there is a need for non-invasive *in vivo* molecular probes to image CXCR4-expressing tumours for better detection, staging and monitoring of aggressive cancers.[13–16] Such imaging agents enable the rapid assessment of patients for expression of specific biomarkers without the need for invasive biopsy procedures that may not always properly capture the heterogeneity of a patient's disease. Furthermore, with the largely poor efficacy of CXCR4 inhibitors in clinical trials, an alternative strategy is to couple the inhibitor with a radiotherapeutic isotope to deliver ionizing β, α, or auger electrons to the sites of the disease.

[0004] LY2510924 (cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr)-NH_2) is a cyclic peptide that is reported to block SDF-1α binding to CXCR4 with an IC_{50} value of 79 pM[17]. It was reported that LY2510924 was able to inhibit growth of non-Hodgkin lymphoma, renal cTbaell carcinoma, lung cancer, colorectal cancer, and breast cancer xenograft models. LY2510924 failed to improve treatment efficacy of carboplatin/etoposide chemotherapy for small cell lung cancer patients[18].

[0005] Many CXCR4 peptide-based inhibitors rely on key amino acid residues that include 1) one or more cationic charged side chain residues to make contact with several anionic residues present on the CXCR4 pocket, 2) a tyrosine residue and 3) a naphthalene-based unnatural amino acid in order to maintain good binding affinity with CXCR4.[19] This is

exemplified in the development of T140, which systematically substituted out each amino acid of a prototype peptide (T22) based on a natural peptide with HIV inhibitory activity *via* CXCR4 antagonism.[19] This has resulted in a number of strong antagonists to CXCR4, including FC131 (which was later repurposed as Pentixafor and Pentixather for imaging and radionuclide therapeutic purposes, respectively) and LY2510924 for radiotheranostic purposes.[20]

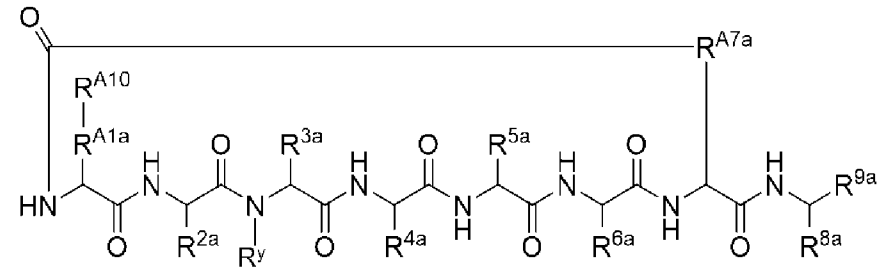
[0006] There is therefore an unmet need in the field for improved CXCR4-targeting compounds, e.g. imaging and therapeutic agents for *in-vivo* diagnosis and treatment, respectively, of diseases/disorders characterized by expression of CXCR4.

[0007] No admission is necessarily intended, nor should it be construed, that any of the preceding information constitutes prior art against the present invention.

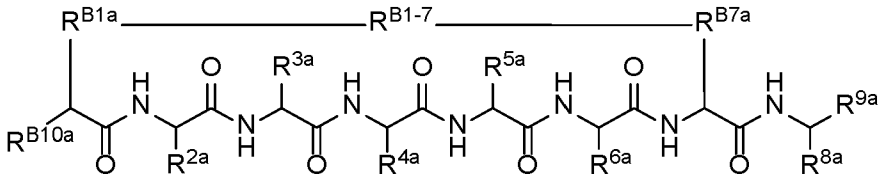
SUMMARY OF THE DISCLOSURE

[0008] The present disclosure relates to compounds useful as imaging agents and/or therapeutic agents.

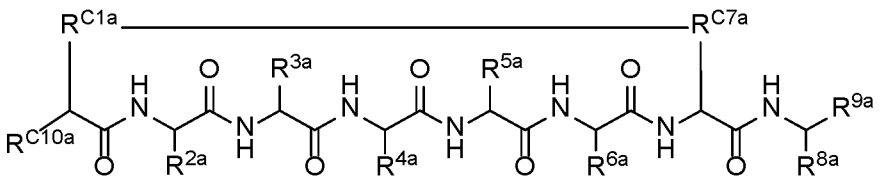
[0009] In some embodiments, the present provides a compound of Formula A, Formula B, or Formula C, or a salt or solvate thereof:



[Formula A];



[Formula B]; or



[Formula C];

wherein:

[0010] R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is

optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0011] R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –$N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0012] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is –$N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0013] R^{5a} is -$(CH_2)_{1-3}$-R^{5b}, wherein 1 carbon in -$(CH_2)_{2-3}$- is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

[0014] phenyl optionally substituted with one or a combination of the following:

[0015] 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, -SR^{5c}, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, –SR^{5c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

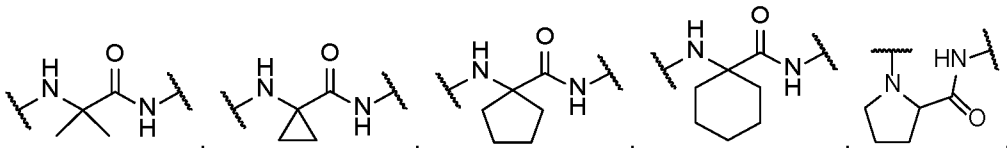
[0016] a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$;

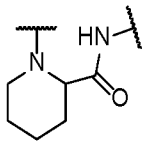
[0017] wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

[0018] either R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -C≡C-$(CH_2)_{1-3}$-OH, -C≡C-$(CH_2)_{1-3}$-SH, -C≡C-$(CH_2)_{1-3}$-NH_2, -C≡C-$(CH_2)_{1-3}$-COOH, -C≡C-$(CH_2)_{1-3}$-$CONH_2$, -C≡C-$(CH_2)_{1-3}$$R^{6b}R^{6c}$, -CH=CH-$(CH_2)_{1-3}$-OH, -CH=CH-$(CH_2)_{1-3}$-SH, -CH=CH-$(CH_2)_{1-3}$-$NH_2$, -CH=CH-$(CH_2)_{1-3}$-COOH, -CH=CH-$(CH_2)_{1-3}$-$CONH_2$, -CH=CH-$(CH_2)_{1-3}$$R^{6b}R^{6c}$, -$CH_2$-$R^{6b}$-OH, -$CH_2$-$R^{6b}$-COOH, -$CH_2$-$(R^{6b})_{1-3}$-$NH_2$, -$CH_2$-$R^{6b}$-$CONH_2$, or -$CH_2$-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-, and wherein R^{6c} is:

[0019] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0020] or -NH-CH(R^{6a})-C(O)-NH- is replaced with:

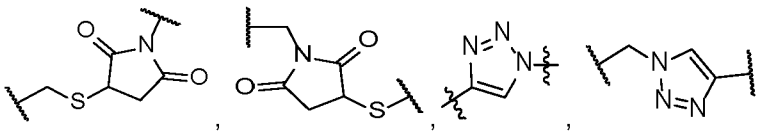

, or


;

[0021] R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

[0022] R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is $-N(R^{8d})_{2\text{-}3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0023] R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, $-CH_2-NH_2$, $-CH_2-OH$, $-CH_2-CH_2-NH_2$, $-R^{9b}-R^{9c}$, or $-R^{9b}$-[linker]-R^{X}_{n1}, wherein:

[0024] R^{9b} is $-CH_2-NH-C(O)-$, $-CH_2-C(O)-$, $-CH_2-O-$, $-C(O)NH-$, $-C(O)-N(CH_3)-$, $-CH_2-NHC(S)-$, $-C(S)NH-$, $-CH_2-N(CH_3)C(S)-$, $-C(O)N(CH_3)-$, $-CH_2-N(CH_3)C(O)-$, $-C(S)N(CH_3)-$, $-CH_2-NHC(S)NH-$, $-CH_2-NHC(O)NH-$, $-CH_2-S-$, $-CH_2-S(O)-$, $-CH_2-S(O)_2-$, $-CH_2-S(O)_2-NH-$, $-CH_2-S(O)-NH-$, $-CH_2-Se-$, $-CH_2-Se(O)-$, $-CH_2-Se(O)_2-$, $-CH_2-NHNHC(O)-$, $-C(O)NHNH-$, $-CH_2-OP(O)(O^-)O-$, $-CH_2$-phosphamide-, $-CH_2$-thiophosphodiester-, $-CH_2-S-$tetrafluorophenyl-S-, 
, or polyethylene glycol; and

[0025] R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

[0026] R^{A10} is absent or -[linker]-R^{X}_{n1};

[0027] when R^{A10} is absent, then R^{A1a} is:

[0028] a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-

(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

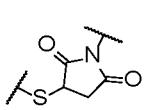
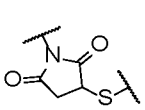
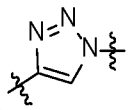
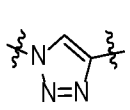
[0029] a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

[0030] $R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

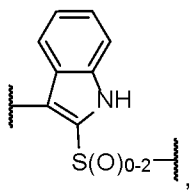
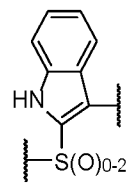
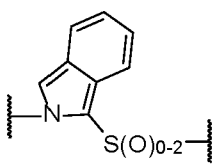
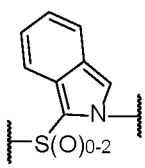
[0031] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

[0032] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

[0033] when R^{A10} is -[linker]-R^X_{n1}, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-$N(CH_3)$-, -NHC(S)-, -C(S)NH-, -$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-,

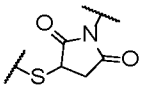
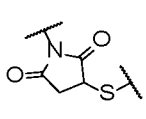
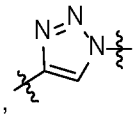
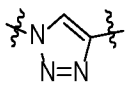

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, or polyethylene glycol;

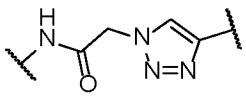
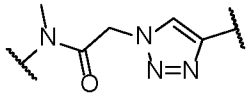
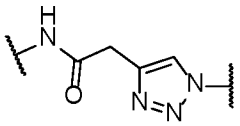
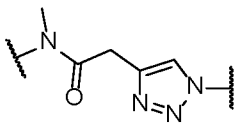
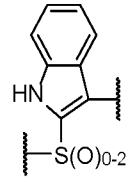
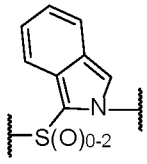
[0034] R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, C_2-C_{10} alkenylenyl, or C_2-C_{10} alkynylenyl, wherein one or more carbons in C_2-C_{10} alkylenyl, alkenylenyl, alkynylenyl are optionally independently replaced with N, S, and/or O heteroatoms;

[0035] R^{B1-7} is

,

,

, or

, wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NO_2, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

[0036] R^{B7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

[0037] R^{B10a} is amine, -NH-$(CH_3)_{1-2}$, -N$(CH_3)_{2-3}$, -NH-C(O)-CH_3, -NH-C(O)-(phenyl), or –R^{B10b}-[linker]-$R^X{}_{n1}$ wherein R^{B10b} is:

[0038] -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S$(O)_2$-, -S$(O)_2$-O-, -S$(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -Se$(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

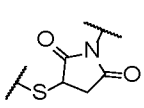
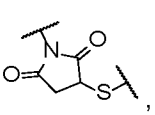
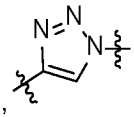
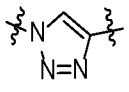
[0039] R^{C1a} is , , , , , or , wherein the indole, the isoindole, and the triazole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

[0040] R^{C7a} is a linear C_1-C_5 alkylenyl, wherein optionally 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

[0041] R^{C10a} is R^{C10b}-R^{C10c}-[linker]-$R^X{}_{n1}$ or R^{C10d}, wherein:

[0042] R^{C10b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

[0043] R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S$(O)_2$-, -S$(O)_2$-O-, -S$(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -Se$(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -

thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

[0044] R^{C10d} is:

[0045] a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

[0046] a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl, wherein 0-3 carbons in C_2-C_{10} alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms; or

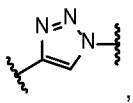
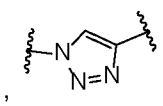
[0047] $R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

[0048] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0049] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

[0050] R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2-3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

[0051] each n1 is independently 0, 1 or 2;

[0052] each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled; wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

[0053] wherein 0-3 peptide backbone amides are N-methylated; and

[0054] wherein C-terminal is optionally amidated.

[0055] In some embodiments, the present disclosure relates a compound selected from Table 2, or a salt or a solvate thereof. In some embodiments, the compound is optionally bound to a radiolabled group, a group capable of being radiolabeled, or an alubumin binder.

[0056] In some embodiments, the present disclosure relates a compound selected from Table 4, or a salt or a solvate thereof.

[0057] In some embodiments of the compounds of the present disclosure, the compound is complexed with a radioisotope.

[0058] In some embodiments, the present disclosure relates to use of any one of the compounds disclosed herein for imaging a CXCR4-expressing tissue in a subject.

[0059] In some embodiments, the present disclosure relates to use of any one of the compounds disclosed herein for imaging an inflammatory condition or disease.

[0060] In some embodiments, the present disclosure provides a method of treating a disease or a condition characterized by expression of CXCR4 in a subject, comprising administering an effective amount of the compound to a subject in need thereof. In some embodments, the disease or condition is a CXCR4-expressing cancer.

[0061] In some embodiments, the present disclosure provides a method of imaging a CXCR4-expresisng tissue in a subject, comprising administering an effective amount of the compound to the subject in need of such imaging.

BRIEF DESCRIPTION OF THE DRAWINGS

[0062] The features of the invention will become apparent from the following description in which reference is made to the appended drawings wherein:

[0063] FIG. 1 shows a representative PET/CT image of [^{68}Ga]Ga-BL34L11 in Z138 tumor-bearing mice at 1 h and 3 h (p.i.). Scale bar is in unit of %ID/g.

[0064] FIG. 2 shows a representative SPECT/CT image of [^{177}Lu]Lu-BL34L11 in Z138 tumor-bearing mice at 1 h, 4 h, 24 h, 72 h, and 120 h (p.i.). Scale bar is in unit of %ID/g.

[0065] FIG. 3 shows a representative SPECT/CT image of [^{177}Lu]Lu-BL34L20 in Z138 tumor-bearing mice at 1 h, 4 h, 24 h, 72 h, and 120 h (p.i.). Scale bar is in unit of %ID/g.

[0066] FIG. 4 shows a representative SPECT/CT image of [^{177}Lu]Lu-crown-BL34 in Z138 tumor-bearing mice at 1 h, 4 h, 24 h, 72 h, and 120 h (p.i.). Scale bar is in unit of %ID/g.

[0067] FIG. 5 shows a representative PET/CT image of [^{68}Ga]Ga-BL34N1 in Z138 tumor-bearing mice at 1 h (p.i.). Scale bar is in unit of %ID/g.

[0068] FIG. 6 shows a representative PET/CT image of [^{68}Ga]Ga-BL34T1 in Z138 tumor-bearing mice at 1 h and 3h (p.i.). Scale bar is in unit of %ID/g.

[0069] FIG. 7 shows a representative SPECT/CT image of [^{177}Lu]Lu-_BL34T1 in Z138 tumor-bearing mice at 4 h, 24 h, 72 h, and 120 h (p.i.). Scale bar is in unit of %ID/g.

[0070] FIG. 8 shows a representative SPECT/CT image of [^{177}Lu]Lu-_BL34L20S in Z138 tumor-bearing mice at 4 h, 24 h, 72 h, and 120 h (p.i.). Scale bar is in unit of %ID/g.

DETAILED DESCRIPTION

[0071] All publications, patents and patent applications, including any drawings and appendices therein are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication, patent or patent application, drawing, or appendix was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

Definitions

[0072] As used herein, the terms "comprising," "having", "including" and "containing," and grammatical variations thereof, are inclusive or open-ended and do not exclude additional, unrecited elements and/or method steps. The term "consisting essentially of" if used herein in connection with a composition, use or method, denotes that additional elements and/or method steps may be present, but that these additions do not materially affect the manner in which the recited composition, method or use functions. The term "consisting of" if used herein in connection with a composition, use or method, excludes the presence of additional elements and/or method steps. A composition, use or method described herein as comprising certain elements and/or steps may also, in certain embodiments consist essentially of those elements and/or steps, and in other embodiments consist of those elements and/or steps, whether or not these embodiments are specifically referred to. A use or method described herein as comprising certain elements and/or steps may also, in certain embodiments consist essentially of those elements and/or steps, and in other embodiments consist of those elements and/or steps, whether or not these embodiments are specifically referred to.

[0073] A reference to an element by the indefinite article "a" does not exclude the possibility that more than one of the elements is present, unless the context clearly requires that there be one and only one of the elements. The singular forms "a", "an", and "the" include plural referents unless the content clearly dictates otherwise. The use of the word "a" or "an" when used herein in conjunction with the term "comprising" may mean "one," but it is also consistent with the meaning of "one or more," "at least one" and "one or more than one."

[0074] Unless otherwise specified, "certain embodiments", "various embodiments", "an embodiment" and similar terms includes the particular feature(s) described for that embodiment either alone or in combination with any other embodiment or embodiments described herein, whether or not the other embodiments are directly or indirectly referenced and regardless of whether the feature or embodiment is described in the context of a method, product, use, composition, compound, *et cetera*.

[0075] As used herein, the terms “treat”, “treatment”, “therapeutic” and the like includes ameliorating symptoms, reducing disease progression, improving prognosis and reducing recurrence (e.g. reducing cancer recurrence).

[0076] As used herein, the term “diagnostic agent” includes an “imaging agent”. As such, a “diagnostic radiometal” includes radiometals that are suitable for use in imaging agents and “diagnostic radioisotope” includes radioisotopes that are suitable for use in imaging agents. Without limitation, dagnostic and imaging agents include compounds comprising at least one fluorescent moiety and/or at least one radioisotope that is suitable for imaging.

[0077] The term “subject” refers to an animal (e.g. a mammal or a non-mammal animal). The subject may be a human or a non-human primate. The subject may be a laboratory mammal (e.g., mouse, rat, rabbit, hamster and the like). The subject may be an agricultural animal (e.g., equine, ovine, bovine, porcine, camelid and the like) or a domestic animal (e.g., canine, feline and the like). In some embodiments, the subject is a human.

[0078] The compounds disclosed herein may also include free-base forms, salts or pharmaceutically acceptable salts thereof. Unless otherwise specified, the compounds claimed and described herein are meant to include all racemic mixtures and all individual enantiomers or combinations thereof, whether or not they are explicitly represented herein.

[0079] The compounds disclosed herein may be shown as having one or more charged groups, may be shown with ionizable groups in an uncharged (e.g. protonated) state or may be shown without specifying formal charges. As will be appreciated by the person of skill in the art, the ionization state of certain groups within a compound (e.g. without limitation, carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid and the like) is dependent, *inter alia*, on the pKa of that group and the pH at that location. For example, but without limitation, a carboxylic acid group (i.e. COOH) would be understood to usually be deprotonated (and negatively charged) at neutral pH and at most physiological pH values, unless the protonated state is stabilized. Likewise, sulfonic acid groups, sulfinic acid groups, and phosphoric acid groups would generally be deprotonated (and negatively charged) at neutral and physiological pH values.

[0080] As used herein, the terms “salt” and “solvate” have their usual meaning in chemistry. As such, when the compound is a salt or solvate, it is associated with a suitable counter-ion. It is well known in the art how to prepare salts or to exchange counter-ions. Generally, such salts can be prepared by reacting free acid forms of these compounds with a stoichiometric amount of a suitable base (e.g. without limitation, Na, Ca, Mg, or K hydroxide, carbonate, bicarbonate, or the like), or by reacting free base forms of these compounds with a stoichiometric amount of a suitable acid. Such reactions are generally carried out in water or in an organic solvent, or in a mixture of the two. Counter-ions may be changed, for example, by ion-exchange techniques such as ion-exchange chromatography. Solvates may be made

any methodology known in the art, e.g. by dissolving the compound in hot solvent (e.g. water or another solvent) followed by cooling and/or evaporation. All zwitterions, salts, solvates and counter-ions are intended, unless a particular form is specifically indicated.

[0081] In certain embodiments, the salt or counter-ion may be pharmaceutically acceptable, for administration to a subject. More generally, with respect to any pharmaceutical composition disclosed herein, non-limiting examples of suitable excipients include any suitable buffers, stabilizing agents, salts, antioxidants, complexing agents, tonicity agents, cryoprotectants, lyoprotectants, suspending agents, emulsifying agents, antimicrobial agents, preservatives, chelating agents, binding agents, surfactants, wetting agents, non-aqueous vehicles such as fixed oils, or polymers for sustained or controlled release. See, for example, Berge et al. 1977. (*J. Pharm Sci*. 66:1-19), or Remington– The Science and Practice of Pharmacy, 21st edition (Gennaro et al editors. Lippincott Williams & Wilkins Philadelphia), each of which is incorporated by reference in its entirety.

[0082] As used herein, the expression "Cy-Cz", where y and z are integers (e.g. C_1-C_{15}, C_1-C_5, and the like), refers to the number of carbons in a compound, R-group or substituent, or refers to the number of carbons plus heteroatoms when a certain number of carbons are specified as being replaced (or optionally replaced) by heteroatoms. Heteroatoms may include any, some or all possible heteroatoms. For example, in some embodiments, the heteroatoms are selected from N, O, S, P and Se. In some embodiments, the heteroatoms are selected from N, S and O. Unless otherwise specified, such embodiments are non-limiting. When replacing a carbon with a heteroatom, it will be understood that the replacements only include those that would be reasonably made by the person of skill in the art. For example, -O-O- linkages are explicitly excluded. The expression "C_1-C_5 … wherein one or more carbons in C_2-C_5 are optionally independently replaced with N, S, and or O heteroatoms" and similar expressions are intended to specify that the C_1 carbon (i.e. the first carbon in the defined group and therefore the carbon directly bonded to the remainder of the compound) is not replaced. Such expressions are also intended to include replacement of one carbon, and replacement of multiple carbons, either with the same heteroatom (e.g. one of N, S, or O) or with a combination of different heteroatoms (e.g. combinations of N, S, and/or O in suitable configurations).

[0083] Unless explicitly stated otherwise, the term "alkyl" includes any reasonable combination of the following: (1) linear or branched; (2) acyclic or cyclic, the latter of which may include multi-cyclic (fused rings, multiple non-fused rings or a combination thereof; and (3) unsubstituted or substituted. In the context of the expression "alkyl, alkenyl or alkynyl" and similar expressions, the "alkyl" would be understood to be a saturated alkyl. As used herein, the term "linear" may be used as it is normally understood to a person of skill in the art and generally refers to a chemical entity that comprises a skeleton or main chain that does not

split off into more than one contiguous chain. Non-limiting examples of linear alkyls include methyl, ethyl, n-propyl, and n-butyl. As used herein, the term "branched" may be used as it is normally understood to a person of skill in the art and generally refers to a chemical entity that comprises a skeleton or main chain that splits off into more than one contiguous chain. The portions of the skeleton or main chain that split off in more than one direction may be linear, cyclic or any combination thereof. Non-limiting examples of a branched alkyl group include tert-butyl and isopropyl.

[0084] The term "alkylenyl" refers to a divalent analog of an alkyl group. In the context of the expression "alkylenyl, alkenylenyl or alkynylenyl", and similar expressions, the "alkylenyl" would be understood to be a saturated alkylenyl.

[0085] As used herein, the term "saturated" when referring to a chemical entity may be used as it is normally understood to a person of skill in the art and generally refers to a chemical entity that comprises only single bonds, and may include linear, branched, and/or cyclic groups. Non-limiting examples of a saturated C_1-C_{20} alkyl group may include methyl, ethyl, n-propyl, i-propyl, sec-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, n-pentyl, i-pentyl, sec-pentyl, t-pentyl, n-hexyl, i-hexyl, 1,2-dimethylpropyl, 2-ethylpropyl, 1-methyl-2-ethylpropyl, l-ethyl-2-methylpropyl, 1,1,2-trimethylpropyl, 1,1,2-triethylpropyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 2-ethylbutyl, 1,3-dimethylbutyl, 2-methylpentyl, 3-methylpentyl, sec-hexyl, t-hexyl, n-heptyl, i-heptyl, sec-heptyl, t-heptyl, n-octyl, i-octyl, sec-octyl, t-octyl, n-nonyl, i-nonyl, sec-nonyl, t-nonyl, n-decyl, i-decyl, sec-decyl, t-decyl, cyclopropanyl, cyclobutanyl, cyclopentanyl, cyclohexanyl, cycloheptanyl, cyclooctanyl, cyclononanyl, cyclodecanyl, and the like. Unless otherwise specified, a C_1-C_{20} alkylenyl therefore encompasses, without limitation, all divalent analogs of the above-listed saturated alkyl groups.

[0086] As used herein, an expression such as "C_3-C_5 alkylenyl, alkenylenyl or alkynylenyl" is understood to mean C_3-C_5 alkylenyl, C_3-C_5 alkenylenyl, or C_3-C_5 alkynylenyl and expression such as "C_1-C_5 alkylenyl, alkenylenyl or alkynylenyl" is understood to mean C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl. Similarly, as used herein, an expression such as "C_5-C_{20} alkyl, alkenyl or alkynyl" is understood to mean C_5-C_{20} alkyl, C_5-C_{20} alkenyl or C_5-C_{20} alkynyl and expression such as "C_1-C_{20} alkyl, alkenyl or alkynyl" is understood to mean C_1-C_{20} alkyl, C_2-C_{20} alkenyl or C_2-C_{20} alkynyl.

[0087] As used herein, the term "unsaturated" when referring to a chemical entity may be used as it is normally understood to a person of skill in the art and generally refers to a chemical entity that comprises at least one double or triple bond, and may include linear, branched, and/or cyclic groups. Non-limiting examples of a C_2-C_{20} alkenyl group may include vinyl, allyl, isopropenyl, l-propene-2-yl, 1-butene-l-yl, l-butene-2-yl, l-butene-3-yl, 2-butene-l-yl, 2-butene-2-yl, octenyl, decenyl, cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, cyclononanenyl, cyclodecanenyl, and the like. Unless otherwise

specified, a C_1-C_{20} alkenylenyl therefore encompasses, without limitation, all divalent analogs of the above-listed alkenyl groups. Non-limiting examples of a C_2-C_{20} alkynyl group may include ethynyl, propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl, and the like. Unless otherwise specified, a C_1-C_{20} alkynylenyl therefore encompasses, without limitation, all divalent analogs of the above-listed alkynyl groups.

[0088] Where it is specified that 1 or more carbons in an alkyl, alkenyl, alkynyl, alkylenyl, alkenylenyl, alkynylenyl, etc., are independently replaced by a heteroatom, the person of skill in the art would understand that various combinations of different heteroatoms may be used. Non-limiting examples of non-aromatic heterocyclic groups include aziridinyl, azetidinyl, diazetidinyl, pyrrolidinyl, pyrrolinyl, piperidinyl, piperazinyl, imidazolinyl, pyrazolidinyl, imidazolydinyl, phthalimidyl, succinimidyl, oxiranyl, tetrahydropyranyl, oxetanyl, dioxanyl, thietanyl, thiepinyl, morpholinyl, oxathiolanyl, and the like. The expression "a linear, branched, and/or cyclic … alkyl, alkenyl or alkynyl" includes, *inter alia*, aryl groups. Unless further specified, an "aryl" group includes both single aromatic rings as well as fused rings containing at least one aromatic ring. Non-limiting examples of C_3-C_{20} aryl groups include phenyl (Ph), pentalenyl, indenyl, naphthyl and azulenyl. Non-limiting examples of C_3-C_{20} aromatic rings with one or more carbons replaced with heteroatoms include pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pirazinyl, quinolinyl, isoquinolinyl, acridinyl, indolyl, isoindolyl, indolizinyl, purinyl, carbazolyl, indazolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, phenanthridinyl, phenazinyl, phenanthrolinyl, perimidinyl, furyl, dibenzofuryl, xanthenyl, benzofuryl, thiophenyl, thianthrenyl, benzothiophenyl, phosphorinyl, phosphinolinyl, phosphindolyl, thiazolyl, oxazolyl, isoxazolyl, and the like. Likewise, the expression "a linear, branched, and/or cyclic … alkylenyl, alkenylenyl or alkynylenyl" includes, *inter alia*, divalent analogs of the above-defined linear, branched, and/or cyclic alkyl, alkenyl or alkynyl groups, including all aryl groups encompassed therein.

[0089] As used herein, the term "substituted" is used as it would normally be understood to a person of skill in the art and generally refers to a compound or chemical entity that has one chemical group replaced with a different chemical group. Unless otherwise specified, a substituted alkyl is an alkyl in which one or more hydrogen atom(s) are independently each replaced with an atom that is not hydrogen. For example, chloromethyl is a non-limiting example of a substituted alkyl, more particularly an example of a substituted methyl. Aminoethyl is another non-limiting example of a substituted alkyl, more particularly an example of a substituted ethyl. Unless otherwise specified, a substituted compound or group (e.g. alkyl, alkylenyl, aryl, and the like) may be substituted with any chemical group reasonable to the person of skill in the art. For example, but without limitation, a hydrogen bonded to a carbon or heteroatom (e.g. N) may be substituted with halide (e.g. F, I, Br, Cl), amine, amide, oxo, hydroxyl, thiol (sulfhydryl), phosphate (or phosphoric acid), phosphonate, sulfate, SO_2H

(sulfinic acid), SO_3H (sulfonic acid), alkyls, aryl, ketones, carboxaldehyde, carboxylic acid, carboxamides, nitriles, guanidino, monohalomethyl, dihalomethyl or trihalomethyl.

[0090] As used herein, the term "guanidino" refers to the group —NHC(=NH)NH_2 or —NHC(=NR)NR_2, wherein each R is independently H or alkyl.

[0091] As used herein, the term "unsubstituted" is used as it would normally be understood to a person of skill in the art. Non-limiting examples of unsubstituted alkyls include methyl, ethyl, tert-butyl, pentyl and the like. The expression "optionally … substituted" is used interchangeably with the expression "unsubstituted or substituted".

[0092] In the structures provided herein, hydrogen may or may not be shown. In some embodiments, hydrogens (whether shown or implicit) may be protium (i.e. ^1H), deuterium (i.e. ^2H) or combinations of ^1H and ^2H. Methods for exchanging ^1H with ^2H are well known in the art. For solvent-exchangeable hydrogens, the exchange of ^1H with ^2H occurs readily in the presence of a suitable deuterium source, without any catalyst. The use of acid, base or metal catalysts, coupled with conditions of increased temperature and pressure, can facilitate the exchange of non-exchangeable hydrogen atoms, generally resulting in the exchange of all ^1H to ^2H in a molecule.

[0093] The compounds disclosed herein incorporate amino acids, e.g. as residues in a peptide chain (linear or branched) or as amino acids that are otherwise part of a compound. Amino acids have both an amino group and a carboxylic acid group, either or both of which can be used for covalent attachment. In attaching to the remainder of the compound, the amino group and/or the carboxylic acid group may be converted to an amide or another structure; e.g. a carboxylic acid group of a first amino acid is converted to an amide (e.g. a peptide bond) when bonded to the amino group of a second amino acid. As such, amino acid residues may have the formula –$N(R^a)R^bC(O)$–, where R^a and R^b are R-groups. R^a will typically be hydrogen or methyl. The amino acid residues of a peptide may comprise typical peptide (amide) bonds and may further comprise bonds between side chain functional groups and the side chain or main chain functional group of another amino acid. For example, the side chain carboxylate of one amino acid residue in the peptide (e.g. Asp, Glu, etc.) may be bonded to and the amine of another amino acid residue in the peptide (e.g. Dap, Dab, Orn, Lys). Further details are provided below. The term "amino acid" includes proteinogenic and nonproteinogenic amino acids. Non-limiting examples of nonproteinogenic amino acids are shown in Table 1 and include: D-amino acids (including without limitation any D-form of the following amino acids), ornithine (Orn), 3-(1-naphtyl)alanine (Nal), 3-(2-naphtyl)alanine (2-Nal), α–aminobutyric acid, norvaline, norleucine (Nle), homonorleucine, beta-(1,2,3-triazol-4-yl)-L-alanine, 1,2,4-triazole-3-alanine, Phe(4-F), Phe(4-Cl), Phe(4-Br), Phe(4-I), Phe(4-NH_2), Phe(4-NO_2), N^{ε}, N^{ε}, N^{ε}-trimethyl-lysine, homoarginine (hArg), 2-amino-4-guanidinobutyric acid (Agb), 2-amino-3-guanidinopropionic acid (Agp), B-alanine, 4-aminobutyric acid, 5-

aminovaleric acid, 6-aminohexanoic acid, 7-aminoheptanoic acid, 8-aminooctanoic acid, 9-aminononanoic acid, 10-aminodecanoic acid, 2-aminooctanoic acid, 2-amino-3-(anthracen-2-yl)propanoic acid, 2-amino-3-(anthracen-9-yl)propanoic acid, 2-amino-3-(pyren-1-yl) propanoic acid, Trp(5-Br), Trp(5-OCH_3), Trp(6-F), Trp(5-OH) or Trp(CHO), 2-aminoadipic acid (2-Aad), 3-aminoadipic acid (3-Aad), propargylglycine (Pra), homopropargylglycine (Hpg), beta-homopropargylglycine (Bpg), 2,3-diaminopropionic acid (Dap), 2,4-diaminobutyric acid (Dab), azidolysine (Lys(N_3)), azido-ornithine (Orn(N_3)), 2-amino-4-azidobutanoic acid Dab(N_3), Dap(N_3), 2-(5'-azidopentyl)alanine, 2-(6'-azidohexyl)alanine, 4-amino-1-carboxymethyl-piperidine (Pip), 4-(2-aminoethyl)-1-carboxymethyl-piperazine (Acp), and tranexamic acid. If not specified as an L- or D-amino acid, an amino acid shall be understood to be an L-amino acid.

[0094] TABLE 1: List of non-limiting examples of non-proteinogenic amino acids.

Any D-amino acid of a proteinogenic amino acid	10-aminodecanoic acid
ornithine (Orn)	2-aminooctanoic acid
3-(1-naphtyl)alanine (Nal)	2-amino-3-(anthracen-2-yl)propanoic acid
3-(2-naphtyl)alanine (2-Nal)	2-amino-3-(anthracen-9-yl)propanoic acid
α–aminobutyric acid	2-amino-3-(pyren-1-yl)propanoic acid
norvaline	Trp(5-Br)
norleucine (Nle)	Trp(5-OCH_3)
homonorleucine	Trp(6-F)
beta-(1,2,3-triazol-4-yl)-L-alanine	Trp(5-OH)
1,2,4-triazole-3-alanine	Trp(CHO)
Phe(4-F) or (4-F)Phe	2-aminoadipic acid (2-Aad)
Phe(4-Cl) or (4-Cl)Phe	3-aminoadipic acid (3-Aad)
Phe(4-Br) or (4-Br)Phe	propargylglycine (Pra)
Phe(4-I) or (4-I)Phe	homopropargylglycine (Hpg)
Phe(4-NH_2) or (4-NH_2)Phe	beta-homopropargylglycine (Bpg)
Phe(4-NO_2) or (4-NO_2)Phe	2,3-diaminopropionic acid (Dap)
(3-I)Tyr	2,4-diaminobutyric acid (Dab)
homoarginine (hArg)	Cysteic acid (CysAcid)
homotyrosine (hTyr)	N^{ε}-isopropyl-lysine (Lys(iPr))
3-(2-phenanthryl)-L-alanine (2-(Ant)Ala)	Arg(Me)
3-(9-phenanthryl)-L-alanine (9-(Ant)Ala)	Arg($Me)_2$ (symmetrical or asymmetrical)
4-(2-aminoethyl)-1-carboxymethyl-piperazine (Acp)	azidolysine (Lys(N_3))
2-(5'-azidopentyl)alanine	azido-ornithine (Orn(N_3))
2-(6'-azidohexyl)alanine	amino-4-azidobutanoic acid Dab(N_3)
2-amino-4-guanidinobutyric acid (Agb)	tranexamic acid
2-amino-3-guanidinopropionic acid (Agp)	4-amino-1-carboxymethyl-piperidine (Pip)

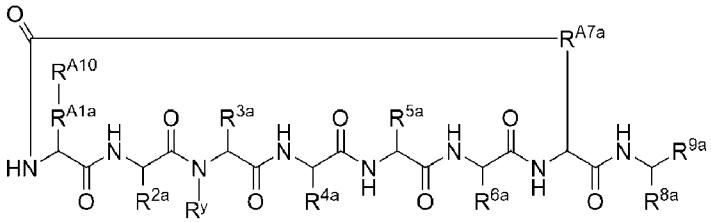
β-alanine	$NH_2(CH_2)_2O(CH_2)_2C(O)OH$
4-aminobutyric acid	$NH_2(CH_2)_2[O(CH_2)_2]_2C(O)OH$
5-aminovaleric acid	$NH_2(CH_2)_2[O(CH_2)_2]_3C(O)OH$
6-aminohexanoic acid	$NH_2(CH_2)_2[O(CH_2)_2]_4C(O)OH$
7-aminoheptanoic acid	$NH_2(CH_2)_2[O(CH_2)_2]_5C(O)OH$
8-aminooctanoic acid	$NH_2(CH_2)_2[O(CH_2)_2]_6C(O)OH$
9-aminononanoic acid	N^{ε}-acetyl-lysine (Lys(Ac))

[0095] As used herein, "peptide backbone amides" refers to the amides (-C(O)-NH-) drawn in the structures of Formula A-I, A-II, A-III, A-III, A-IV, B, or C, for example, including the amide bond between carbon atoms bonded to R^{2a}, R^{3a}, R^{4a}, R^{5a}, R^{6a}, R^{A7a}, R^{B7a}, and R^{C7a}. One or more peptide backbone amides can be methylated or N-methylated, unless otherwise discussed herein. For example, the amide bond between carbon atoms bonded to R^{2a}, R^{3a}, R^{4a}, R^{5a}, R^{6a}, R^{A7a}, R^{B7a}, and R^{C7a} can methylated (-C(O)-NCH_3-).

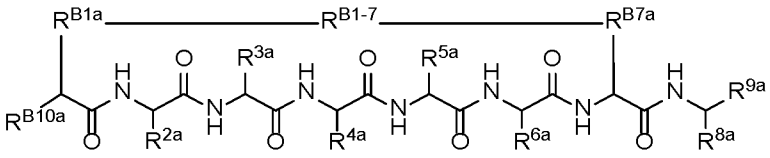
[0096] The wavy line "〰" symbol shown through or at the end of a bond in a chemical formula (e.g. in the definition L^1) is intended to define the R group on one side of the wavy line, without modifying the definition of the structure on the opposite side of the wavy line. Where an R group is bonded on two or more sides (e.g. certain definitions of X^1), any atoms shown outside the wavy lines are intended to clarify orientation of the R group. As such, only the atoms between the two wavy lines constitute the definition of the R group. When atoms are not shown outside the wavy lines, or for a chemical group shown without wavy lines but does have bonds on multiple sides (e.g. –C(O)NH–, and the like.), the chemical group should be read from left to right matching the orientation in the formula that the group relates to (e.g. for formula $–R^a–R^b–R^c–$, the definition of R^b as –C(O)NH– would be incorporated into the formula as $–R^a–$C(O)NH$–R^c–$ not as $–R^a–$NHC(O)$–R^c–$).

Compounds

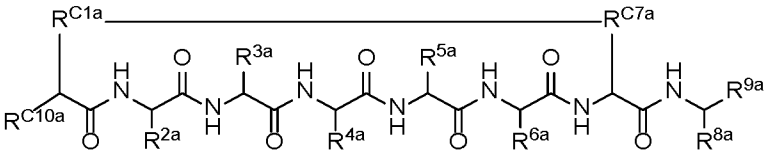
[0097] In various aspects, there is disclosed a compound of Formula A, B, or C, or a salt or solvate of Formula A, B, or C:



[Formula A];



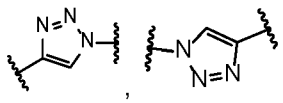
[Formula B];



[Formula C];

R-groups are defined below;

wherein 0-3 peptide backbone amides are independently replaced with



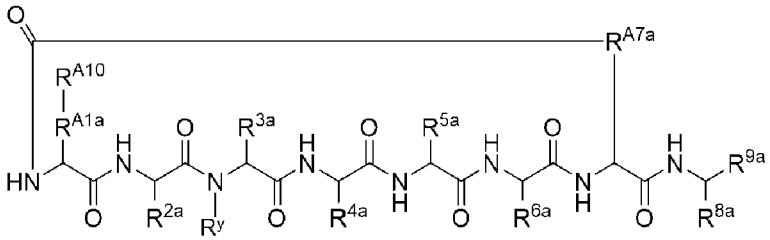
, amidine, or thioamide;

wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

[0098] In some embodiments, the compound has the structure of Formula A. In some embodiments, the compound is a salt of Formula A. In some embodiments, the compound is a solvate of Formula A.

[0099] In some embodiments, the compound has the structure of Formula A, or a salt or



solvate thereof: [Formula A], wherein:

[0100] R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -N_3, -CN, or -SR^{2c}, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0101] R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or

more N, S, and/or O heteroatoms, wherein R^{3c} is $–N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0102] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0103] R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein 1 carbon in $-(CH_2)_{2-3}-$ is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

[0104] phenyl optionally substituted with one or a combination of the following:

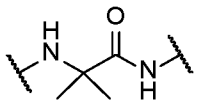
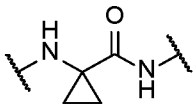
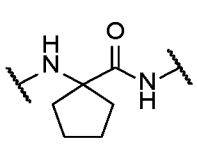
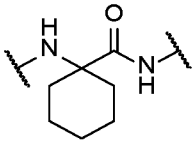
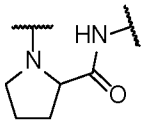
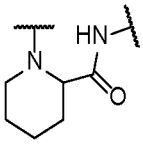
[0105] 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $-SR^{5c}$, $-N_3$, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $–SR^{5c}$, $-N_3$, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

[0106] a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$;

[0107] wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

[0108] either R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-C≡C-(CH_2)_{1-3}-OH$, $-C≡C-(CH_2)_{1-3}-SH$, $-C≡C-(CH_2)_{1-3}-NH_2$, $-C≡C-(CH_2)_{1-3}-COOH$, $-C≡C-(CH_2)_{1-3}-CONH_2$, $-C≡C-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH=CH-(CH_2)_{1-3}-OH$, $-CH=CH-(CH_2)_{1-3}-SH$, $-CH=CH-(CH_2)_{1-3}-NH_2$, $-CH=CH-(CH_2)_{1-3}-COOH$, $-CH=CH-(CH_2)_{1-3}-CONH_2$, $-CH=CH-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH_2-R^{6b}-OH$, $-CH_2-R^{6b}-COOH$, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH_2$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-, and wherein R^{6c} is:

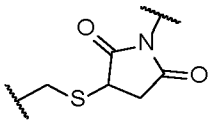
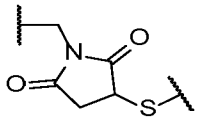
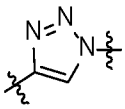
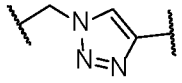
[0109] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0110] or $-NH-CH(R^{6a})-C(O)-NH-$ is replaced with:  ,  ,  ,  ,  , or  ;

[0111] R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

[0112] R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is –$N(R^{8d})_{2\text{-}3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0113] R^{9a} is -$C(O)NH_2$, -C(O)-OH, -CH_2-$C(O)NH_2$, -CH_2-C(O)-OH, -CH_2-NH_2, -CH_2-OH, -CH_2-CH_2-NH_2, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^X_{n1}, wherein:

[0114] R^{9b} is -CH_2-NH-C(O)-, -CH_2-C(O)-, -CH_2-O-, -C(O)NH-, -C(O)-$N(CH_3)$-, -CH_2-NHC(S)-, -C(S)NH-, -CH_2-$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -CH_2-$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -CH_2-NHC(S)NH-, -CH_2-NHC(O)NH-, -CH_2-S-, -CH_2-S(O)-, -CH_2-$S(O)_2$-, -CH_2-$S(O)_2$-NH-, -CH_2-S(O)-NH-, -CH_2-Se-, -CH_2-Se(O)-, -CH_2-$Se(O)_2$-, -CH_2-NHNHC(O)-, -C(O)NHNH-, -CH_2-OP(O)(O^-)O-, -CH_2-phosphamide-, -CH_2-thiophosphodiester-, -CH_2-S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

[0115] R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

[0116] R^{A10} is absent or -[linker]-R^X_{n1};

[0117] when R^{A10} is absent, then R^{A1a} is:

[0118] a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -$N(CH_3)_{2\text{-}3}$, -S-CH_3, or -O-CH_3;

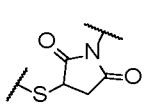
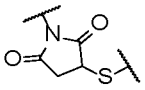
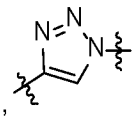
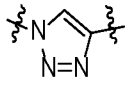
[0119] a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

[0120] $R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

[0121] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

[0122] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

[0123] when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-,

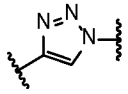
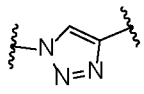

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, or polyethylene glycol;

[0124] R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2\text{-}3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

[0125] each n1 is independently 0, 1 or 2;

[0126] each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

[0127] wherein 0-3 peptide backbone amides are independently replaced with


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, amidine, or thioamide;

[0128] wherein 0-3 peptide backbone amides are N-methylated; and

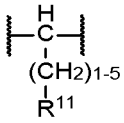
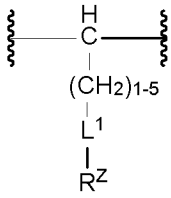
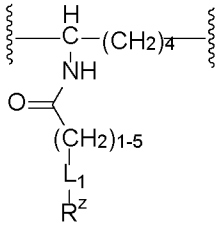
[0129] wherein C-terminal is optionally amidated.

[0130] In some embodiments of the compounds of Formula A, the compound does not have the combination: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and R^{6a} is H.

[0131] In some embodiments of the compounds of Formula A,

[0132] R^{A10} is -[linker]-$R^X{}_{n1}$;

[0133] the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

[0134] X^1 is each independently $-CH_2-$, , , or ;

[0135] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, $-N(CH_3)C(O)-$, or $-C(O)N(CH_3)-$;

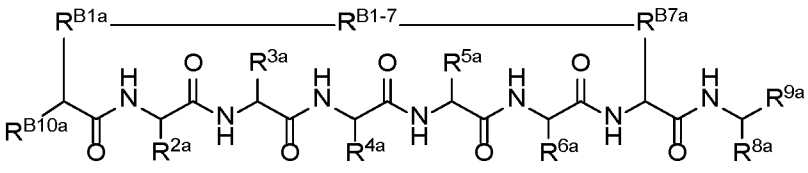
[0136] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0137] R^Z is each independently an albumin binder.

[0138] In some embodiments of the compounds of Formula A, R^y is $R^{3e}R^{3f}$.

[0139] In some embodiments of the compounds of Formula A, the compound comprises an albumin binder.

[0140] In some embodiments, the compound has the structure of Formula B. In some embodiments, the compound is a salt of Formula B. In some embodiments, the compound is a solvate of Formula B.

[0141] In some embodiments, the compound has the structure of Formula B, or a salt or solvate thereof:  [Formula B], wherein:

[0142] R^{2a} is $-(CH_2)-(R^{2b})-$(phenyl), wherein R^{2b} is absent, $-CH_2-$, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, $-N_3$, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, $-N_3$, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0143] R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or

more N, S, and/or O heteroatoms, wherein R^{3c} is $–N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0144] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0145] R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein 1 carbon in $-(CH_2)_{2-3}-$ is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

[0146] phenyl optionally substituted with one or a combination of the following:

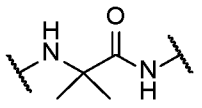
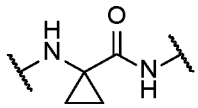
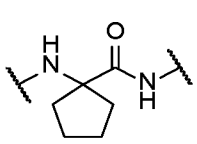
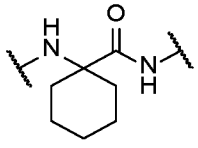
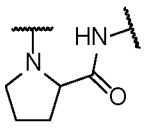
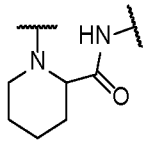
[0147] 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $-SR^{5c}$, $-N_3$, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $–SR^{5c}$, $-N_3$, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

[0148] a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$;

[0149] wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

[0150] either R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-C≡C-(CH_2)_{1-3}-OH$, $-C≡C-(CH_2)_{1-3}-SH$, $-C≡C-(CH_2)_{1-3}-NH_2$, $-C≡C-(CH_2)_{1-3}-COOH$, $-C≡C-(CH_2)_{1-3}-CONH_2$, $-C≡C-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH=CH-(CH_2)_{1-3}-OH$, $-CH=CH-(CH_2)_{1-3}-SH$, $-CH=CH-(CH_2)_{1-3}-NH_2$, $-CH=CH-(CH_2)_{1-3}-COOH$, $-CH=CH-(CH_2)_{1-3}-CONH_2$, $-CH=CH-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH_2-R^{6b}-OH$, $-CH_2-R^{6b}-COOH$, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH_2$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-, and wherein R^{6c} is:

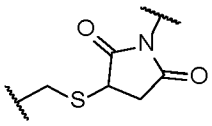
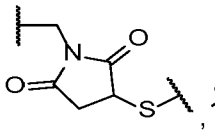
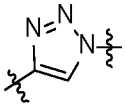
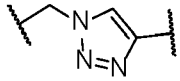
[0151] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0152] or $-NH-CH(R^{6a})-C(O)-NH-$ is replaced with: , , , , , or ;

[0153] R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is –

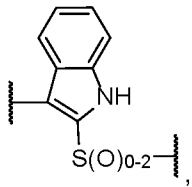
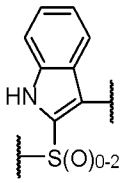
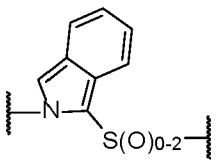
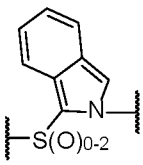
$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0154] R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, $-CH_2-NH_2$, $-CH_2-OH$, $-CH_2-CH_2-NH_2$, $-R^{9b}-R^{9c}$, or $-R^{9b}$-[linker]-$R^X{}_{n1}$, wherein:

[0155] R^{9b} is $-CH_2-NH-C(O)-$, $-CH_2-C(O)-$, $-CH_2-O-$, $-C(O)NH-$, $-C(O)-N(CH_3)-$, $-CH_2-NHC(S)-$, $-C(S)NH-$, $-CH_2-N(CH_3)C(S)-$, $-C(O)N(CH_3)-$, $-CH_2-N(CH_3)C(O)-$, $-C(S)N(CH_3)-$, $-CH_2-NHC(S)NH-$, $-CH_2-NHC(O)NH-$, $-CH_2-S-$, $-CH_2-S(O)-$, $-CH_2-S(O)_2-$, $-CH_2-S(O)_2-NH-$, $-CH_2-S(O)-NH-$, $-CH_2-Se-$, $-CH_2-Se(O)-$, $-CH_2-Se(O)_2-$, $-CH_2-NHNHC(O)-$, $-C(O)NHNH-$, $-CH_2-OP(O)(O^-)O-$, $-CH_2$-phosphamide-, $-CH_2$-thiophosphodiester-, $-CH_2-S-$ tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

[0156] R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

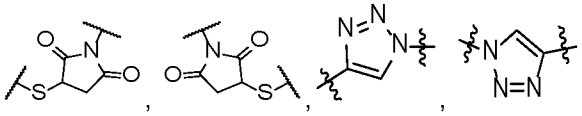
[0157] R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, C_2-C_{10} alkenylenyl, or C_2-C_{10} alkynylenyl, wherein one or more carbons in C_2-C_{10} alkylenyl, alkenylenyl, alkynylenyl are optionally independently replaced with N, S, and/or O heteroatoms;

[0158] R^{B1-7} is , , , or , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, $-O-R^{B1-7b}$, -CO-, -COOH, $-CONH_2$, -CN, -O-aryl, $-NH_2$, $-NHR^{B1-7b}$, N_3, $-NO_2$, -NH, -CHO, and/or $-R^{B1-7b}$, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

[0159] R^{B7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

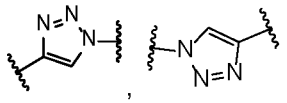
[0160] R^{B10a} is amine, $-NH-(CH_3)_{1-2}$, $-N(CH_3)_{2-3}$, $-NH-C(O)-CH_3$, -NH-C(O)-(phenyl), or $-R^{B10b}$-[linker]-$R^X{}_{n1}$ wherein R^{B10b} is:

[0161] $-NH-C(O)-$, $-C(O)-$, $-O-$, $-C(O)NH-$, $-C(O)-N(CH_3)-$, $-NHC(S)-$, $-C(S)NH-$, $-N(CH_3)C(S)-$, $-C(O)N(CH_3)-$, $-N(CH_3)C(O)-$, $-C(S)N(CH_3)-$, $-NHC(S)NH-$, $-NHC(O)NH-$, $-S-$, $-S(O)-$, $-S(O)-O-$, $-S(O)_2-$, $-S(O)_2-O-$, $-S(O)_2-NH-$, $-S(O)-NH-$, $-Se-$, $-Se(O)-$, $-Se(O)_2-$, -

NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , or polyethylene glycol;

[0162] each n1 is independently 0, 1 or 2;

[0163] each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

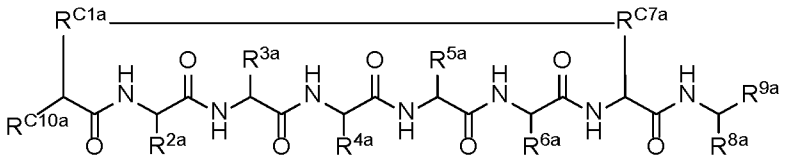
[0164] wherein 0-3 peptide backbone amides are independently replaced with , amidine, or thioamide;

[0165] wherein 0-3 peptide backbone amides are N-methylated; and

[0166] wherein C-terminal is optionally amidated.

[0167] In some embodiments, the compound has the structure of Formula C. In some embodiments, the compound is a salt of Formula C. In some embodiments, the compound is a solvate of Formula C.

[0168] In some embodiments, the compound has the structure of Formula C, or a salt or solvate thereof:



[Formula C], wherein:

[0169] R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0170] R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –$N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0171] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S,

and/or O heteroatoms, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0172] R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein 1 carbon in $-(CH_2)_{2-3}-$ is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

[0173] phenyl optionally substituted with one or a combination of the following:

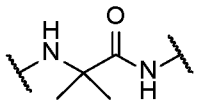
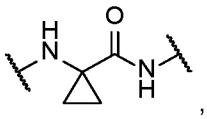
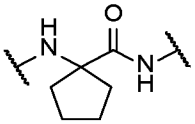
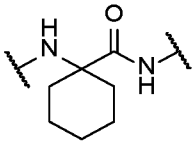
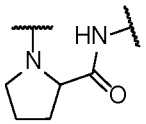
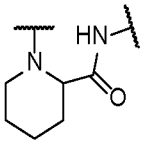
[0174] 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $-SR^{5c}$, $-N_3$, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $–SR^{5c}$, $-N_3$, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

[0175] a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$;

[0176] wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

[0177] either R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-C≡C-(CH_2)_{1-3}-OH$, $-C≡C-(CH_2)_{1-3}-SH$, $-C≡C-(CH_2)_{1-3}-NH_2$, $-C≡C-(CH_2)_{1-3}-COOH$, $-C≡C-(CH_2)_{1-3}-CONH_2$, $-C≡C-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH=CH-(CH_2)_{1-3}-OH$, $-CH=CH-(CH_2)_{1-3}-SH$, $-CH=CH-(CH_2)_{1-3}-NH_2$, $-CH=CH-(CH_2)_{1-3}-COOH$, $-CH=CH-(CH_2)_{1-3}-CONH_2$, $-CH=CH-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH_2-R^{6b}-OH$, $-CH_2-R^{6b}-COOH$, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH_2$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-, and wherein R^{6c} is:

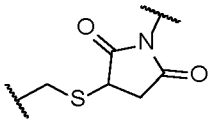
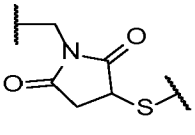
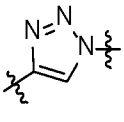
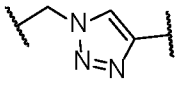
[0178] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0179] or $-NH-CH(R^{6a})-C(O)-NH-$ is replaced with:  ,  ,  ,  ,  , or  ;

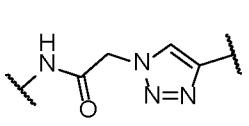
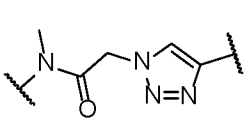
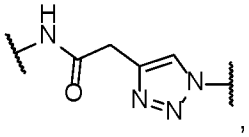
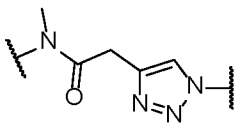
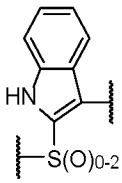
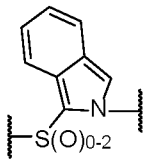
[0180] R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

[0181] R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0182] R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, -CH_2-NH_2, -CH_2-OH, -CH_2-CH_2-NH_2, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-$R^X{}_{n1}$, wherein:

[0183] R^{9b} is -CH_2-NH-C(O)-, -CH_2-C(O)-, -CH_2-O-, -C(O)NH-, -C(O)-N(CH_3)-, -CH_2-NHC(S)-, -C(S)NH-, -CH_2-N(CH_3)C(S)-, -C(O)N(CH_3)-, -CH_2-N(CH_3)C(O)-, -C(S)N(CH_3)-, -CH_2-NHC(S)NH-, -CH_2-NHC(O)NH-, -CH_2-S-, -CH_2-S(O)-, -CH_2-$S(O)_2$-, -CH_2-$S(O)_2$-NH-, -CH_2-S(O)-NH-, -CH_2-Se-, -CH_2-Se(O)-, -CH_2-$Se(O)_2$-, -CH_2-NHNHC(O)-, -C(O)NHNH-, -CH_2-OP(O)(O^-)O-, -CH_2-phosphamide-, -CH_2-thiophosphodiester-, -CH_2-S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

[0184] R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

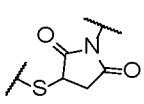
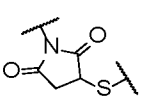
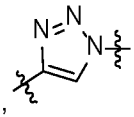
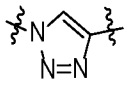
[0185] R^{C1a} is , , , , , or , wherein the indole, the isoindole, and the triazole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

[0186] R^{C7a} is a linear C_1-C_5 alkylenyl, wherein optionally 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

[0187] R^{C10a} is R^{C10b}-R^{C10c}-[linker]-$R^X{}_{n1}$ or R^{C10d}, wherein:

[0188] R^{C10b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

[0189] R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -

thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

[0190] R^{C10d} is:

[0191] a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

[0192] a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl, wherein 0-3 carbons in C_2-C_{10} alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms; or

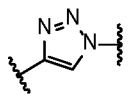
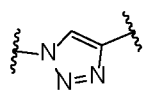
[0193] $R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

[0194] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0195] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

[0196] each n1 is independently 0, 1 or 2;

[0197] each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

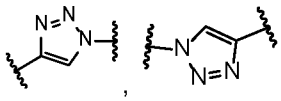
[0198] wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

[0199] wherein 0-3 peptide backbone amides are N-methylated; and

[0200] wherein C-terminal is optionally amidated.

[0201] In some embodiments of the compounds of Formula A, B, and/or C, the compound comprises an albumin binder.

[0202] In some embodiments of the compounds of Formula A, B, and/or C, R^{9a} is R^{9b}-[linker] R^{x}_{n1}. In some embodiments of the compounds of Formula A, B, and/or C, R^{3a} is C_1-C_5 alkyl. In some embodiments of the compounds of Formula A, B, and/or C, at least one peptide backbone amides are N-methylated. In some embodiments of the compounds of Formula A, B, and/or C, at least one peptide backbone amides are replaced with an amidine.

[0203] In some embodiments of the compounds of Formula A, B, and/or C, 1 peptide backbone amide is replaced with  , amidine, or thioamide. In some embodiments, two peptide backbone amides are replaced. In some embodiments, three peptide backbone amides are replaced. In some embodiments, zero peptide backbone amides are replaced.

[0204] In some embodiments of the compounds of Formula A, B, and/or C, at least one peptide backbone is N-methylated. In some embodiments, one peptide backbone amide is N-methylated. In some embodiments, two peptide backbone amides are N-methylated. In some embodiments, three peptide backbone amides are N-methylated. In some embodiments, zero peptide backbone amides are N-methylated.

[0205] In some embodiments of the compounds of Formula A, B, and/or C, at least one peptide backbone amide is replaced with an amidine. In some embodiments, one peptide backbone amide is replaced with an amidine. In some embodiments, two peptide backbone amides are each replaced with an amidine. In some embodiments, three peptide backbone amides are each replated with an amidine. In some embodiments, zero peptide backbone amides are each replaced with an amidine.

[0206] In some embodiments, the peptide backbone carbonyl between R^{3a} and R^{4a}; between R^{4a} and R^{5a}; or between R^{5a} and R^{6a} is replaced with an imino (-CH(R^{3a})-C(=N)-NH-CH(R^{4a})-, -CH(R^{4a})-C(=N)-NH-CH(R^{5a})- or -CH(R^{5a})-C(=N)-NH-CH(R^{6a})-). In some embodiments, the peptide backbone carbonyl between R^{3a} and R^{4a} is replaced with an imino ((-CH(R^{3a})-C(=N)-NH-CH(R^{4a})-). In some embodiments, the peptide backbone carbonyl between R^{4a} and R^{5a} is replaced with an imino (-CH(R^{4a})-C(=N)-NH-CH(R^{5a})-). the peptide backbone carbonyl between R^{5a} and R^{6a} is replaced with an imino (-CH(R^{5a})-C(=N)-NH-CH(R^{6a})-).

[0207] In some embodiments of the compounds of Formula A, B, and/or C, R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with

halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group.

[0208] In some embodiments of the compounds of Formula A, B, and/or C, R^{2b} is absent. In some embodiments, R^{2b} is -CH_2-. In some embodiments, R^{2b} is -NH-. In some embodiments, R^{2b} is -S-. In some embodiments, R^{2b} is -O-.

[0209] In some embodiments of the compounds of Formula A, B, and/or C, R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent or -CH_2-, wherein the phenyl is 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl. In some embodiments, the phenyl is 4-substituted with -NH_2. In some embodiments, the phenyl is 4-substituted with -NO_2. In some embodiments, the phenyl is 4-substituted with –OH. In some embodiments, the phenyl is 4-substituted with –SH. In some embodiments, the phenyl is 4-substituted with -O-phenyl. In some embodiments, the phenyl is 3,5-unsubstituted. In some embodiments, the phenyl is 3-substituted. In some embodiments, phenyl is 5-substituted. In some embodiments, the phenyl is 3,5-substituted. In some embodiments, the halogen substituent is iodine. The 3,5-substituents may be the same or different (e.g. different halogens, or a mix of halogen and –OH).

[0210] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{2a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a Tyr residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a Phe residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a (4-NO_2)-Phe residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a (4-NH_2)-Phe residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a hTyr residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a (3-I)Tyr residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a Glu residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a Gln residue. In some embodiments, -NH-CH(R^{2a})-C(O)- forms a D-Tyr residue.

[0211] In some embodiments of the compounds of Formula A, B, and/or C, R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, wherein 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –N(R^{3d})$_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl.

[0212] In some embodiments of the compounds of Formula A, B, and/or C, R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, wherein 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –N(R^{3d})$_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl.

[0213] In some embodiments of the compounds of Formula A, B, and/or C, R^{3b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl (i.e. no heteroatoms). In some embodiments, R^{3b}

comprises a single heteroatom (N, S or O) in any one of C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl. In some embodiments, R^{3b} is a linear C_1-C_5 alkylenyl.

[0214] In some embodiments of the compounds of Formula A, B, and/or C, R^{3c} is guanidino. In some embodiments, R^{3c} is $-N(R^{3d})_{2-3}$. In some embodiments, R^{3c} is $-N(R^{3d})_{2-3}$ wherein each R^{3d} is a linear or branched C_1-C_3 alkyl. In some embodiments, R^{3c} is $-N(R^{3d})_{2-3}$ wherein each R^{3d} is methyl. In some embodiments, R^{3c} is $-N(R^{3d})_{2-3}$ wherein each R^{3d} is independently -H or methyl. In some embodiments, R^{3c} is $-NH_2$ or $-NH_3$.

[0215] In some embodiments of the compounds of Formula A, B, and/or C, R^{3a} is C_1-C_5 alkyl. In some embodiments, R^{3a} is methyl. In some embodiments, R^{3a} is ethyl. In some embodiments, R^{3a} is propyl. In some embodiments, R^{3a} is butyl. In some embodiments, R^{3a} is pentyl.

[0216] In some embodiments of the compounds of Formula A, $-NR^y$-$CH(R^{3a})$-C(O)- forms an L-amino acid residue. In some embodiments, $-NR^y$-$CH(R^{3a})$-C(O)- forms a D-amino acid residue. In some embodiments, $-NR^y$-$CH(R^{3a})$-C(O)- forms a Lys(iPr) residue. In some embodiments, $-NR^y$-$CH(R^{3a})$-C(O)- forms an $Arg(Me)_2$ (asymmetrical) residue. In some embodiments, $-NR^y$-$CH(R^{3a})$-C(O)- forms an Arg(Me) residue.

[0217] In some embodiments of the compounds of Formula A, NR^y-$CH(R^{3a})$-C(O)- is -NH-$CH(R^{3a})$-C(O)-. In some embodiments, -NH-$CH(R^{3a})$-C(O)- forms an L-amino acid residue. In some embodiments, -NH-$CH(R^{3a})$-C(O)- forms a D-amino acid residue. In some embodiments, -NH-$CH(R^{3a})$-C(O)- forms a Lys(iPr) residue. In some embodiments, -NH-$CH(R^{3a})$-C(O)- forms an $Arg(Me)_2$ (asymmetrical) residue. In some embodiments, -NH-$CH(R^{3a})$-C(O)- forms an Arg(Me) residue.

[0218] In some embodiments of the compounds of Formula A, NR^y-$CH(R^{3a})$-C(O)- is $-NCH_3$-$CH(R^{3a})$-C(O)-. In some embodiments, $-NCH_3$-$CH(R^{3a})$-C(O)- forms an L-amino acid residue. In some embodiments, $-NCH_3$-$CH(R^{3a})$-C(O)- forms a D-amino acid residue. In some embodiments, $-NCH_3$-$CH(R^{3a})$-C(O)- forms a Lys(iPr) residue. In some embodiments, $-NCH_3$-$CH(R^{3a})$-C(O)- forms an $Arg(Me)_2$ (asymmetrical) residue. In some embodiments, $-NCH_3$-$CH(R^{3a})$-C(O)- forms an Arg(Me) residue.

[0219] In some embodiments of Formula A, R^y is hydrogen, C_1-C_5 alkyl, or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is $–N(R^{3g})_{2-3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl.

[0220] In some embodiments of Formula A, R^y is hydrogen. In some embodiments of Formula A, R^y is a C_1-C_5 alkyl. In some embodiments, R^y is methyl.

[0221] In some embodiments of Formula A, R^y is $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is $–N(R^{3g})_{2-3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl. In some embodiments, R^y is (C_{1-5} alkylenyl)-NH(C_{2-3} alkyl). In some embodiments, R^y is (C_4 alkylenyl)-NH(isopropyl).

[0222] In some embodiments of the compounds of Formula B and/or C, -NH-CH(R^{3a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{3a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{3a})-C(O)- forms an Arg(Me)$_2$ (asymmetrical) residue. In some embodiments, -NH-CH(R^{3a})-C(O)- forms an Arg(Me) residue.

[0223] In some embodiments of the compounds of Formula A, B, and/or C, R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is –N(R^{4d})$_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl.

[0224] In some embodiments of the compounds of Formula A, B, and/or C, R^{4b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl (i.e. no heteroatoms). In some embodiments, R^{4b} comprises a single heteroatom (N, S or O) in any one of C_2-C_5. In some embodiments, R^{4b} is a linear C_1-C_5 alkylenyl.

[0225] In some embodiments of the compounds of Formula A, B, and/or C, R^{4c} is guanidino. In some embodiments, R^{4c} is -N(R^{4d})$_{2-3}$. In some embodiments, R^{4c} is -N(R^{4d})$_{2-3}$ wherein each R^{4d} is a linear or branched C_1-C_3 alkyl. In some embodiments, R^{4c} is -N(R^{4d})$_{2-3}$ wherein each R^{4d} is methyl. In some embodiments, R^{4c} is -N(R^{4d})$_{2-3}$ wherein each R^{4d} is independently -H or methyl. In some embodiments, R^{4c} is -NH_2 or -NH_3.

[0226] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{4a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{4a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{4a})-C(O)- forms a D-Arg residue. In some embodiments, -NH-CH(R^{4a})-C(O)- forms a D-hArg residue.

[0227] In some embodiments, of Formula A, B, and/or C, the carbonyl of -NH-CH(R^{4a})-C(O)- is replaced with an imino to form -NH-CH(R^{4a})-C(=NH)-. In some embodiments, -NH-CH(R^{4a})-C(=NH)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{4a})-C(=NH)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{4a})-C(O)- forms a D-Arg residue. In some embodiments, -NH-CH(R^{4a})-C(=NH)- forms a D-hArg residue.

[0228] In some embodiments of the compounds of Formula A, B, and/or C, R^{5a} is -(CH_2)$_{1-3}$-R^{5b}, wherein 1 carbon in -(CH_2)$_{2-3}$- is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

phenyl optionally substituted with one or a combination of the following: 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, -SR^{5c}, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, –SR^{5c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and independently optionally substituted with one or a combination of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$;

wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group.

[0229] In some embodiments of the compounds of Formula A, B, and/or C, R^{5a} is -CH_2-R^{5b}. In some embodiments, R^{5a} is -CH_2-CH_2-R^{5b}. In some embodiments, R^{5a} is -CH_2-CH_2-CH_2-R^{5b}.

[0230] In some embodiments of the compounds of Formula A, B, and/or C, R^{5b} is phenyl optionally substituted with one or a combination of the following: 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, -SR^{5c}, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, –SR^{5c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH. In some embodiments, R^{5b} is phenyl optionally substituted with one or a combination of the following: 4-substituted with -NH_2, -NO_2, -OH, -SH, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH. In some embodiments, the phenyl is 4-unsubstituted. In some embodiments, the phenyl is 4-substituted with -NH_2. In some embodiments, the phenyl is 4-substituted with -NO_2. In some embodiments, the phenyl is 4-substituted with –OH. In some embodiments, the phenyl is 4-substituted with -OR^{5c}. In some embodiments, the phenyl is 4-substituted with –SH. In some embodiments, the phenyl is 4-substituted with -SR^{5c}. In some embodiments, the phenyl is 4-substituted with -N_3. In some embodiments, the phenyl is 4- substituted with -CN. In some embodiments, the phenyl is 4-substituted with -O-phenyl. In some embodiments, each R^{5c} is independently a C_1-C_3 linear or branched alkyl group. In some embodiments, each R^{5c} is methyl. In some embodiments, the phenyl is 3-unsubstituted. In some embodiments, the phenyl is 3-substituted with halogen. In some embodiments, the phenyl is 3-substituted with –OH. In some embodiments, the phenyl is 5-substituted with halogen. In some embodiments, the phenyl is 5-substituted with -OH. In some embodiments, the halogen is iodine. In some embodiments, the -O-phenyl ring is unsubstituted. In some embodiments, the -O-phenyl ring is 4-substituted. In some embodiments, the -O-phenyl ring is 3-substituted. In some embodiments, the -O-phenyl ring is 5-substituted.

[0231] In some embodiments of the compounds of Formula A, B, and/or C, R^{5b} is a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally independently substituted with one or a combination of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$. In some embodiments, each R^{5c} is independently a C_1-C_3 linear or branched alkyl group. In some embodiments, each R^{5c} is methyl. In some embodiments, R^{5b} is a fused bicyclic or fused tricyclic aryl group wherein

0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally independently substituted with one or a combination of halogen, -OH, and/or amino. In some embodiments, R^{5b} is a fused bicyclic or fused tricyclic aryl group optionally independently substituted with one or a combination of halogen, -OH, and/or amino. In some embodiments, R^{5b} is a fused bicyclic or fused tricyclic aryl group optionally independently substituted with 0-3 groups selected from halogen, -OH, and/or amino. In some embodiments, R^{5b} is a fused bicyclic or fused tricyclic aryl group. In some embodiments, R^{5b} excludes 9-linked anthracenyl. In some embodiments, each ring in the fused bicyclic or fused tricyclic aryl group independently has 4, 5 or 6 ring carbons, wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms; such embodiments may be substituted or unsubstituted as defined above.

[0232] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{5a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-(Ant)Ala residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a Trp residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a hTyr residue. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a Tyr residue.

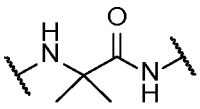
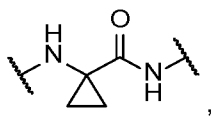
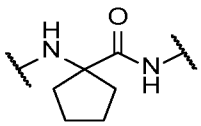
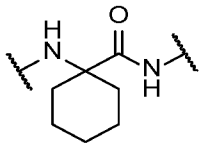
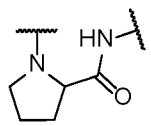
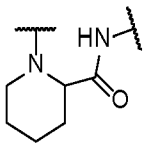
[0233] In some embodiments of Formula A, B, and/or C, the carbonyl of -NH-CH(R^{5a})-C(O)- is replaced with an imino to form -NH-CH(R^{5a})-C(=NH)-. In some embodiments of Formula A, B, and/or C, the backbone amide of -NH-CH(R^{5a})-C(O)- is replaced with an amidine to form -NH-CH(R^{5a})-C(=NH)-. In some embodiments, -NH-CH(R^{5a})-C(O)- forms an L-amino acid residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a D-amino acid residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-(Ant)Ala residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a Trp residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a hTyr residue and the backbone amide is replaced with an amidine. In some embodiments, -NH-CH(R^{5a})-C(O)- forms a Tyr residue and the backbone amide is replaced with an amidine.

[0234] In some embodiments of the compounds of Formula A, B, and/or C, either:

(a) R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -C≡C-$(CH_2)_{1-3}$-OH, -C≡C-$(CH_2)_{1-3}$-SH, -C≡C-$(CH_2)_{1-3}$-NH_2, -C≡C-$(CH_2)_{1-3}$-COOH, -C≡C-$(CH_2)_{1-3}$-$CONH_2$, -C≡C-$(CH_2)_{1-3}R^{6b}R^{6c}$, -CH=CH-$(CH_2)_{1-3}$-OH, -CH=CH-$(CH_2)_{1-3}$-SH, -CH=CH-$(CH_2)_{1-3}$-NH_2, -CH=CH-$(CH_2)_{1-3}$-

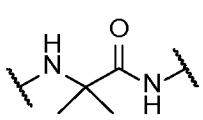
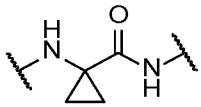
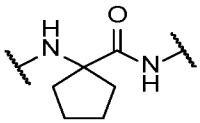
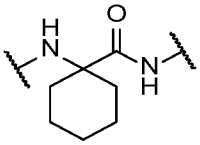
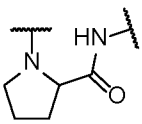
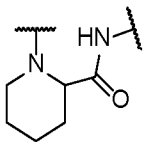
COOH, -CH=CH-$(CH_2)_{1-3}$-$CONH_2$, -CH=CH-$(CH_2)_{1-3}R^{6b}R^{6c}$, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-, and wherein R^{6c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

(b) -NH-CH(R^{6a})-C(O)-NH- is replaced with: , , , , , or .

[0235] In some embodiments of the compounds of Formula A, B, and/or C, R^{6a} is H. In some embodiments, R^{6a} is methyl. In some embodiments, R^{6a} is ethyl. In some embodiments, R^{6a} is -C≡CH. In some embodiments, R^{6a} is -$CH=CH_2$. In some embodiments, R^{6a} is -CH_2-R^{6b}-OH. In some embodiments, R^{6a} is -CH_2-R^{6b}-COOH. In some embodiments, R^{6a} is -CH_2-$(R^{6b})_{1-3}$-NH_2. In some embodiments, R^{6a} is -CH_2-R^{6b}-$CONH_2$. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}$-OH. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}$-SH. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}$-NH_2. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}$-COOH. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}$-$CONH_2$. In some embodiments, R^{6a} is -C≡C-$(CH_2)_{1-3}R^{6b}R^{6c}$. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}$-OH. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}$-SH. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}$-NH_2. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}$-COOH. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}$-$CONH_2$. In some embodiments, R^{6a} is -CH=CH-$(CH_2)_{1-3}R^{6b}R^{6c}$. Each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-. In some embodiments, R^{6b} is absent. In some embodiments, R^{6b} is -CH_2-.

[0236] In some embodiments of the compounds of Formula A, B, and/or C, R^{6a} is H, methyl, ethyl, -C≡CH, -$CH=CH_2$, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$. In some embodiments, R^{6a} is -CH_2-$R^{6b}R^{6c}$. Each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-. In some embodiments, R^{6b} is absent. In some embodiments, R^{6b} is -CH_2-. In some embodiments, R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; in some embodiments, the ring is unsubstituted. In some embodiments, R^{6c} is a 5 or 6 membered aryl, optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; in some embodiments, the aryl is unsubstituted.

[0237] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{6a})-C(O)-NH- is replaced with: , , , or . In some embodiments, -NH-CH(R^{6a})-C(O)-NH- is replaced with: , or .

[0238] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{6a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a His residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-His residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Glu residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Gln residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Ala residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Phe residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Ser residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Dab residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Dap residue.

[0239] In some embodiments of the compounds of Formula A, B, and/or C, R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl.

[0240] In some embodiments of the compounds of Formula A, B, and/or C, R^{8b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl (i.e. no heteroatoms). In some embodiments, R^{8b} comprises a single heteroatom (N, S or O) in any one of C_2-C_5. In some embodiments, R^{8b} is a linear C_1-C_5 alkylenyl.

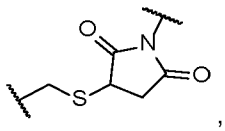
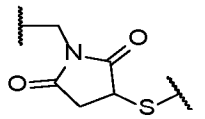
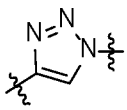
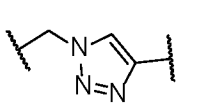
[0241] In some embodiments of the compounds of Formula A, B, and/or C, R^{8c} is guanidino. In some embodiments, R^{8c} is -$N(R^{8d})_{2-3}$. In some embodiments, R^{8c} is -$N(R^{8d})_{2-3}$ wherein each R^{8d} is a linear or branched C_1-C_3 alkyl. In some embodiments, R^{8c} is -$N(R^{8d})_{2-3}$ wherein each R^{8d} is methyl. In some embodiments, R^{8c} is -$N(R^{8d})_{2-3}$ wherein each R^{8d} is independently -H or methyl. In some embodiments, R^{8c} is -NH_2 or -NH_3.

[0242] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{8a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{8a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. As

used herein, in the expression "-NH-CH(R^{8a})-C(O)-" made about Formula A, A-I, A-II, A-III, A-IV, B, and/or C, it is understood that the -C(O)- portion is part of R^{9a} definition. For example, in some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms an L amino acid residue, a D-amino acid residue, or a Lys(iPr) residue.

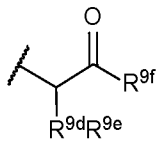
[0243] In some embodiments of the compounds of Formula A, B, and/or C, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms an amino acid residue. In some embodiments, the amino acid residue formed by -NH-CH(R^{8a})- together with -C(O)- from R^{9a} is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue which is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr)-NH_2.

[0244] In some embodiments of the compounds of Formula A, B, and/or C, R^{9a} is: -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, -CH_2-NH_2, -CH_2-OH, -CH_2-CH_2-NH_2, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^{X}_{n1}, wherein:

R^{9b} is -CH_2-NH-C(O)-, -CH_2-C(O)-, -CH_2-O-, -C(O)NH-, -C(O)-N(CH_3)-, -CH_2-NHC(S)-, -C(S)NH-, -CH_2-N(CH_3)C(S)-, -C(O)N(CH_3)-, -CH_2-N(CH_3)C(O)-, -C(S)N(CH_3)-, -CH_2-NHC(S)NH-, -CH_2-NHC(O)NH-, -CH_2-S-, -CH_2-S(O)-, -CH_2-$S(O)_2$-, -CH_2-$S(O)_2$-NH-, -CH_2-S(O)-NH-, -CH_2-Se-, -CH_2-Se(O)-, -CH_2-$Se(O)_2$-, -CH_2-NHNHC(O)-, -C(O)NHNH-, -CH_2-OP(O)(O^-)O-, -CH_2-phosphamide-, -CH_2-thiophosphodiester-, -CH_2-S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid.

[0245] In some embodiments of the compounds of Formula A, B, and/or C, R^{9a} is: -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH. In some embodiments, R^{9a} is -R^{9b}-R^{9c} wherein R^{9b} is –C(O)NH–.

[0246] In some embodiments of the compounds of Formula A, B, and/or C, R^{9c} is , wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with N, S, and/or O heteroatoms, wherein R^{9e} is

carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-CH_3, -N(CH_3)$_2$, -S-CH_3, -O-CH_3, and phenyl, and wherein R^{9f} is amino or –OH. In some embodiments, R^{9d} is a linear or branched C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl (i.e. no heteroatoms). In some embodiments, R^{9d} is a linear or branched C_1-C_5 alkylenyl.

[0247] In some embodiments of the compounds of Formula A, B, and/or C, R^{9a} is -R^{9b}-[linker]-$R^X{}_{n1}$. In some of these embodiments, R^{9b} is -C(O)NH-.

[0248] In some embodiments of the compounds of Formula A, B, and/or C: R^{9a} is -C(O)NH_2, -C(O)-OH, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-$R^X{}_{n1}$; and R^{9b} is -C(O)NH-, -C(O)-N(CH_3)-, -C(O)N(CH_3)-, or -C(O)NHNH-.

[0249] In some embodiments of the compounds of Formula A, R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms. In some embodiments, R^{A7a} is a linear C_1-C_5 alkylenyl (i.e. no heteroatoms). In some embodiments, R^{A7a} is a linear C_1-C_5 alkylenyl in which one carbon in C_2-C_5 is a heteroatom selected from N, S or O. In some embodiments, R^{A7a} is –CH_2–. In some embodiments, R^{A7a} is –CH_2-CH_2–.

[0250] In some embodiments, -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{A7a})-C(O)- forms an L-amino acid residue.

[0251] In some embodiments, -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue and R^{A7a} is C_1-C_3 alkyenyl. In some embodiments, -NH-CH(R^{A7a})-C(O)- forms an L-amino acid residue and R^{A7a} is C_1-C_3 alkyenyl.

[0252] In some embodiments of the compounds of Formula A, R^{A10} is absent or -[linker]-$R^X{}_{n1}$.

[0253] In some embodiments of the compounds of Formula A, when R^{A10} is absent, then R^{A1a} is:

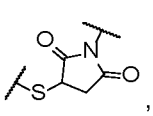
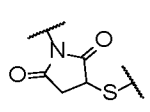
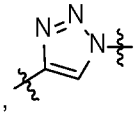
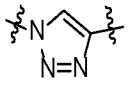
a linear C_1-C_5 alkyl, alkenyl, or alkynyl, wherein 0-2 carbons in C_2-C_5 are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-(CH_3)$_{1\text{-}2}$, -NH_2-CH_3, -N(CH_3)$_{2\text{-}3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group.

[0254] In some embodiments of the compounds of Formula A, when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, polyethylene glycol, , , , or .

[0255] In some embodiments of the compounds of Formula A, -NH-CH(R^{A1a})-C(O)- forms an L-amino acid residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a D-amino acid residue.

[0256] In some embodiments of the compounds of Formula A, R^{A10} is absent.

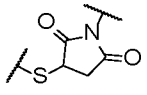
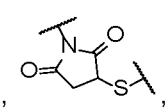
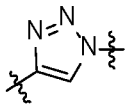
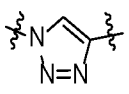
[0257] In some of embodiments of the compounds of Formula A, where R^{A10} is absent, R^{A1a} is a linear C_1-C_5 alkyl, alkenyl, or alkynyl, optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -$N(CH_3)_{2\text{-}3}$, -S-CH_3, or -O-CH_3. In some of embodiments where R^{A10} is absent, R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -$N(CH_3)_{2\text{-}3}$, -S-CH_3, or -O-CH_3.

[0258] In some of embodiments of the compounds of Formula A, where R^{A10} is absent, R^{A1a} is a branched C_1-C_{10} alkyl, alkenyl, or alkynyl. In some of embodiments where R^{A10} is absent, R^{A1a} is a branched C_1-C_{10} alkyl.

[0259] In some of embodiments of the compounds of Formula A, where R^{A10} is absent, R^{A1a} is $R^{A1b}R^{A1c}$. In some embodiments, R^{A1b} is a linear C_1-C_3 alkylenyl. In some embodiments, R^{A1c} is a 5 or 6 membered aromatic ring wherein 0-4 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-4 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen. In some embodiments, R^{A1c} is a fused bicyclic or fused tricyclic aryl group wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-6 groups independently selected from

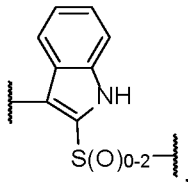
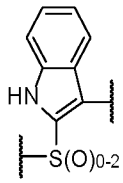
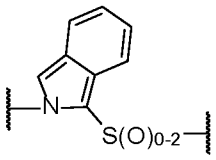
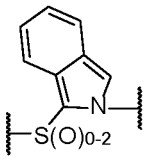
halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or N(R^{A1d})$_2$. In some embodiments, R^{A1d} is methyl. In some embodiments, each ring in the fused bicyclic or fused tricyclic aryl group independently has 4, 5 or 6 ring carbons, wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms; such embodiments may be substituted or unsubstituted as defined above.

[0260] In some embodiments of the compounds of Formula A, -NH-CH(R^{A1a})-C(O)- forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, a Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue. n some embodiments of the compounds of Formula A, -NH-CH(R^{A1a})-C(O)- forms an L-Phe residue, an L-1-Nal residue, an L-2-Nal residue, an L-Tyr residue, an L-Trp residue, an L-Lys residue, an L-hLys residue, an L-Lys(Ac) residue, an L-Dap residue, an L-Dab residue, or an L-Orn residue. In some embodiments of the compounds of Formula A, -NH-CH(R^{A1a})-C(O)- forms a Phe residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a 1-Nal residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a 2-Nal residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Tyr residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Trp residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Lys residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a hLys residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Lys(Ac) residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Dap residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Dab residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms an Orn residue.

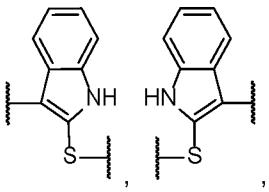
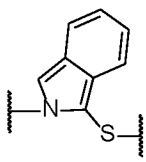
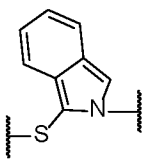
[0261] In some embodiments of the compounds of Formula A, R^{A10} is -[linker]-R$^{X}_{n1}$ and R^{A1a} is R^{A1e}R^{A1f}. In some embodiments, R^{A1e} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl. In some embodiments, R^{A1e} is a linear C_1-C_5 alkylenyl. In some embodimetns, R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH$_3$)-, -NHC(S)-, -C(S)NH-, -N(CH$_3$)C(S)-, -C(O)N(CH$_3$)-, -N(CH$_3$)C(O)-, -C(S)N(CH$_3$)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S(O)$_2$-, -S(O)$_2$-NH-, -S(O)-NH-, -NHNHC(O)-, -C(O)NHNH-, polyethylene glycol, , , , or .

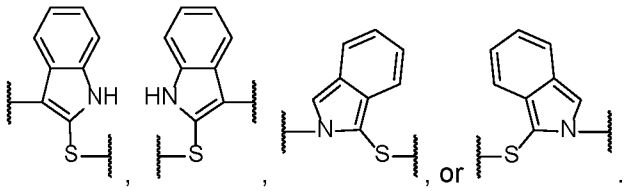
[0262] All embodiments described herein for Formula A can be embodiments for Formula A-I, Formula A-II, Formula III and/or Formula A-IV to the extent the definitions are encompassed by Formula A-I, Formula A-II, Formula III, and/or Formula IV.

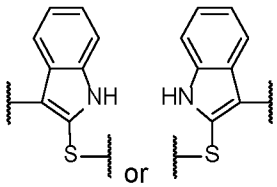
[0263] In some embodiments of the compounds of Formula B, R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, alkenylenyl, or alkynylenyl, wherein one or more carbons in C_2-C_{10} are optionally independently replaced with N, S, and/or O heteroatoms.

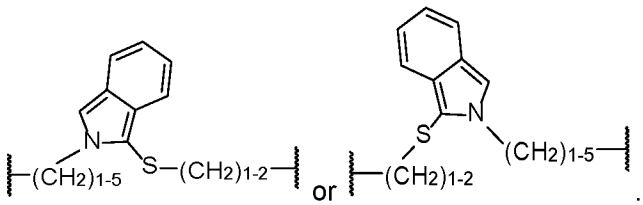
[0264] In some embodiments of the compounds of Formula B, R^{B1-7} is: , , , or , wherein the indole and the isoindole are optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NO_2, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, alkenyl, or alkynyl. In some embodiments, the indole and the isoindole are not substituted. In some embodiments, the indole and the isoindole are substituted with 1-3 groups selected from -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}. In some embodiments, each R^{C1b} is methyl. In some embodiments, the aryl is a 5 or 6 membered aromatic ring.

[0265] In some embodiments of the compounds of Formula B, R^{B7a} is a linear C_1-C_5 alkylenyl wherein optionally 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms. In some embodiments, R^{B7a} is a linear C_1-C_5 alkylenyl (i.e. no heteroatoms). In some embodiments, R^{B7a} is a linear C_1-C_5 alkylenyl in which one carbon in C_2-C_5 is a heteroatom selected from N, S or O. In some embodiments, R^{B7a} is $–CH_2–$. In some embodiments, R^{B7a} is -CH_2-CH_2-. In some embodiments, -NH-CH(R^{C7a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{C7a})-C(O)- forms an L-amino acid residue.

[0266] In some embodiments of the compounds of Formula B, R^{B1-7} is , , or , wherein the indole and the isoindole are optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NO_2, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, alkenyl, or alkynyl. In some embodiments, the indole and the isoindole are substituted with 1-3 groups selected from -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}. In some embodiments, each R^{C1b} is

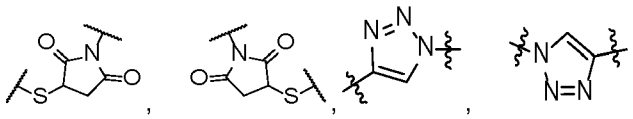
methyl. In some embodiments, the aryl is a 5 or 6 membered aromatic ring. In some embodiments, R^{B1-7} is .

[0267] In some embodiments of the compounds of Formula B, R^{B1a} is $-(CH_2)_{1-2}$-, R^{B1-7} is  , and R^{B7a} is $-(CH_2)_{1-2}$-.

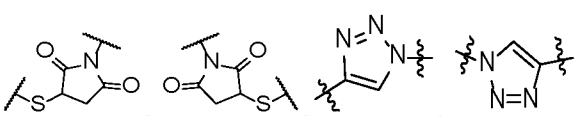
[0268] In some embodiments of the compounds of Formula B, R^{B1a}-R^{B1-7}-R^{B7a} is .

[0269] In some embodiments of the compounds of Formula B, -NH-CH(R^{B7a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{B7a})-C(O)- forms an L-amino acid residue.

[0270] In some embodiments of the compounds of Formula B, R^{B10a} is: amine, -NH-$(CH_3)_{1-2}$, -N$(CH_3)_{2-3}$, -NH-C(O)-CH_3, -NH-C(O)-(phenyl), or $-R^{B10b}$-[linker]-R^{X}_{n1} wherein R^{B10b} is:

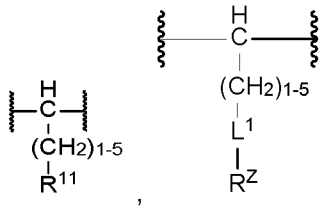
-NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , or polyethylene glycol.

[0271] In some embodiments of the compounds of Formula B, R^{B10a} is: amine, -NH-$(CH_3)_{1-2}$, -N$(CH_3)_{2-3}$, -NH-C(O)-CH_3, or -NH-C(O)-(phenyl).

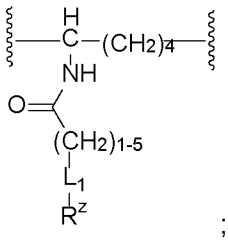
[0272] In some embodiments of the compounds of Formula B, R^{B10a} is -R^{B10b}-[linker]-R^{X}_{n1}. In some of these embodiments R^{B10b} is: -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -NHNHC(O)-, -C(O)NHNH-, , or

polyethylene glycol. In some embodiments, R^{B10a} is -NHC(O)-[linker]-R^{X}_{n1} or -N(CH_3)C(O)-[linker]-R^{X}_{n1}.

[0273] In some embodiments, the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;



[0274] X^1 is each independently -CH_2-, , , or



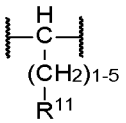
;

[0275] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, or –C(O)N(CH_3)–;

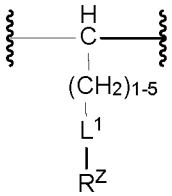
[0276] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0277] R^Z is each independently an albumin binder.

[0278] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

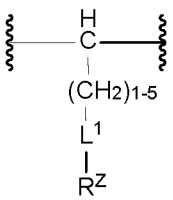
[0279] X^{1a} is  ;

[0280] L^{1a} is –NH– or –NHC(O)–;

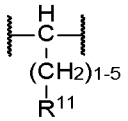
[0281] X^{1b} is  ; and

[0282] L^{1b} is –NH– or –NHC(O)–.

[0283] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

[0284] X^{1a} is  ;

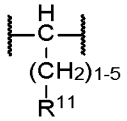
[0285] L^{1a} is –NH– or –NHC(O)–;



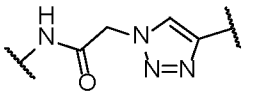
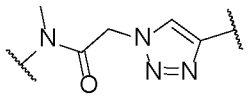
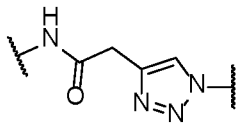
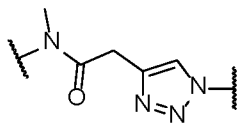
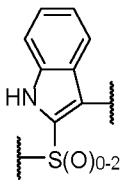
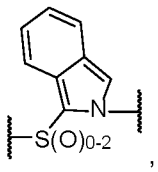
[0286] X^{1b} is ; and

[0287] L^{1b} is –NH– or –NHC(O)–.

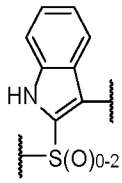
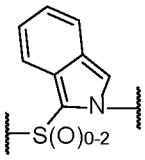
[0288] In some embodiments, R^{B10a} is -NHC(O)-[linker]-R^{X}_{n1}, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$,



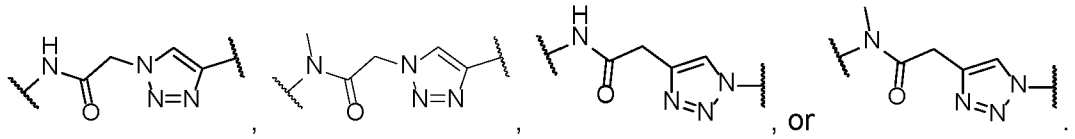
[0289] X^{1a} is C_1-C_2 alkenyl; L^{1a} is -NH-C(O); X^{1b} is ; and L^{1b} is -NH-, and R^{11} is independently carboxylic acid, sulfonic acid, sulfinic acid, or phosphoric acid. In some embodiments, R^{11} is sulfonic acid (-SO_3H).

[0290] In some embodiments of the compounds of Formula C, R^{C1a} is: , , , , , or , wherein the indole, the isoindole, and the triazole rings are optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, alkenyl, or alkynyl, provided that the compound of Formula C is not cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr)-NH_2, cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr)-NH_2, cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, and cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr)-NH_2. In some embodiments, the indole and the isoindole are not substituted. In some embodiments, the indole and the isoindole are substituted with 1-3 groups selected from -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}. In some embodiments, each R^{C1b} is methyl. In some embodiments, the aryl is a 5 or 6 membered aromatic ring.

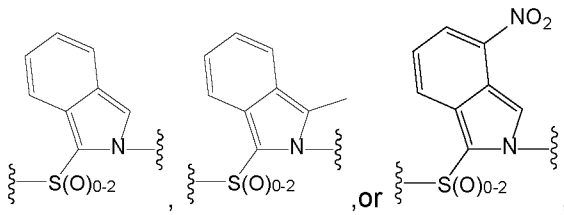
[0291] In some embodiments of the compounds of Formula C, R^{C1a} is:



, wherein the indole and the isoindole are optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, alkenyl, or alkynyl, provided that the compound of Formula C is not cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr)-NH_2, cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr)-NH_2, cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, and cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr)-NH_2. In some embodiments, the indole and the isoindole are not substituted. In some embodiments, the indole and the isoindole are substituted with 1-3 groups selected from -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or -R^{C1b}. In some embodiments, each R^{C1b} is methyl. In some embodiments, the aryl is a 5 or 6 membered aromatic ring.

[0292] In some embodiments of the compounds of Formula C, R^{C1a} is:


, or .

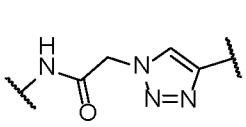
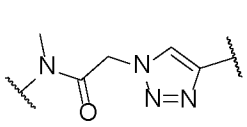
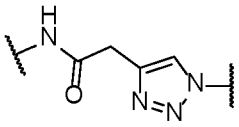
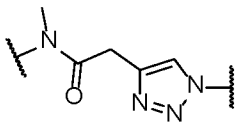
[0293] In some embodiments of the compounds of Formula C, R^{C1a} is:


, provided that the compound of Formula C is not cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr)-NH_2, cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr)-NH_2, cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, and cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr)-NH_2.

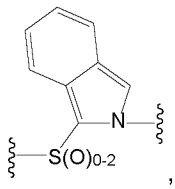
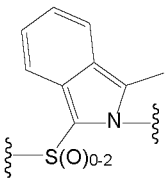
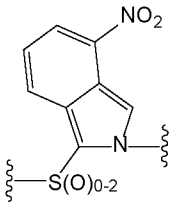
[0294] In some embodiments of the compounds of Formula C, R^{C7a} is a linear C_1-C_5 alkylenyl wherein optionally 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S,

and/or O heteroatoms. In some embodiments, R^{C7a} is a linear C_1-C_5 alkylenyl (i.e. no heteroatoms). In some embodiments, R^{C7a} is a linear C_1-C_2 alkylenyl. In some embodiments, R^{C7a} is a linear C_1-C_5 alkylenyl in which one carbon in C_2-C_5 is a heteroatom selected from N, S or O. In some embodiments, R^{C7a} is $–(CH_2)_{1\text{-}2}–$. In some embodiments, -NH-CH(R^{C7a})-C(O)- forms a D-amino acid residue. In some embodiments, -NH-CH(R^{C7a})-C(O)- forms an L-amino acid residue.

[0295] In some embodiments of compounds of Formula C, R^{C1a} is:

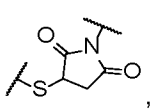
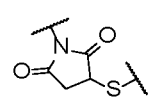
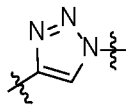
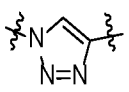

, 
, 
, or 
, and R^{C7a} is a linear C_1-C_2 alkylenyl.

[0296] In some embodiments of compounds of Formula C, R^{C1a} is:


, 
,or 
and R^{C7a} is a linear C_1-C_2 alkylenyl, provided that the compound of Formula C is not cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr)-NH_2, cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr)-NH_2, cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, and cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr)-NH_2.

[0297] In some embodiments of the compounds of Formula C, R^{C10a} is R^{C10b}-R^{C10c}-[linker]-$R^X{}_{n1}$ or R^{C10d}, wherein:

R^{C10b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with N, S, and/or O heteroatoms;

R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, 
, 
, 
, 
, or polyethylene glycol; and

R^{C10d} is:

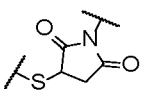
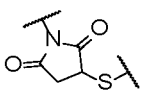
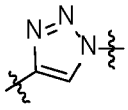
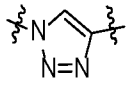
a linear C_1-C_5 alkyl, alkenyl, or alkynyl, wherein 0-2 carbons in C_2-C_5 are independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -$N(CH_3)_{2\text{-}3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by N, S, and/or O heteroatoms; or

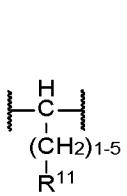
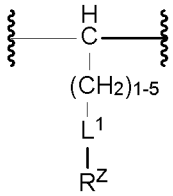
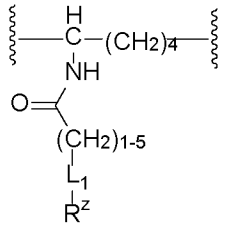
$R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl.

[0298] In some embodiments of the compounds of Formula C, R^{C10a} is R^{C10b}-R^{C10c}-[linker]-$R^X{}_{n1}$. In some embodiments, R^{C10b} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl. In some embodiments, R^{C10b} is a linear C_1-C_5 alkylenyl. In some embodiments, R^{C10c} is: -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol. In some embodiments, R^{C10c} is –NHC(O)- or -N(CH_3)C(O)-.

[0299] In some embodiments, the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

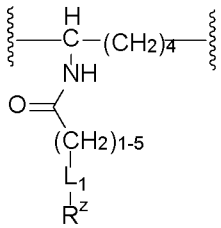
[0300] X^1 is each independently -CH_2-, , , or ;

[0301] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)C(O)$–, or –$C(O)N(CH_3)$–;

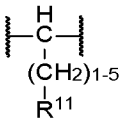
[0302] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0303] R^Z is each independently an albumin binder.

[0304] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

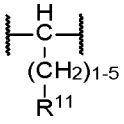
[0305] X^{1a} is ;

[0306] L^{1a} is –NH– or –NHC(O)–;

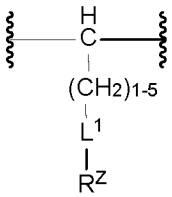
[0307] X^{1b} is ; and

[0308] L^{1b} is –NH– or –NHC(O)–.

[0309] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

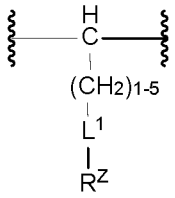
[0310] X^{1a} is ;

[0311] L^{1a} is –NH– or –NHC(O)–;

[0312] X^{1b} is ; and

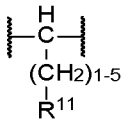
[0313] L^{1b} is –NH– or –NHC(O)–.

[0314] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;



[0315] X^{1a} is ;

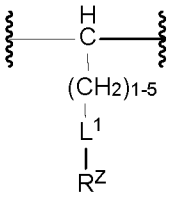
[0316] L^{1a} is –NH– or –NHC(O)–;



[0317] X^{1b} is ; and

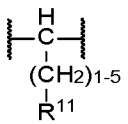
[0318] L^{1b} is –NH– or –NHC(O)–.

[0319] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;



[0320] X^{1a} is ;

[0321] L^{1a} is –NH– or –NHC(O)–;



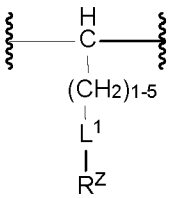
[0322] X^{1b} is ;

[0323] L^{1b} is –NH– or –NHC(O)–;

[0324] X^{1c} is $–CH_2–$; and

[0325] L^{1c} is –NH– or –NHC(O)–.

[0326] In some embodiments, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;

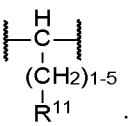


[0327] X^{1a} is ;

[0328] L^{1a} is –NH– or –NHC(O)–;

[0329] X^{1b} is $–CH_2–$;

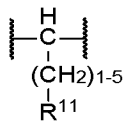
[0330] L^{1b} is –NH– or –NHC(O)–;



[0331] X^{1c} is ; and

[0332] L^{1c} is –NH– or –NHC(O)–.

[0333] In some embodiments, R^{C10a} is -NHC(O)-[linker]-R^{X}_{n1}, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$,



[0334] X^{1a} is C_1-C_2 alkenyl; L^{1a} is -NH-C(O); X^{1b} is ; and L^{1b} is -NH-, and R^{11} is independently carboxylic acid, sulfonic acid, sulfinic acid, or phosphoric acid.

[0335] In some embodiments, R^{11} is sulfonic acid (-SO_3H).

[0336] In some embodiments of the compounds of Formula C, R^{C10a} is R^{C10d}.

[0337] In some embodiments of the compounds of Formula C, R^{C10d} is a linear C_1-C_5 alkyl, alkenyl, or alkynyl, wherein 0-2 carbons in C_2-C_5 are independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from the group consisting of: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, and -O-CH_3.

[0338] In some embodiments of the compounds of Formula C, R^{C10d} is a linear C_1-C_5 alkyl, alkenyl, or alkynyl, optionally C-substituted with a single substituent selected from the group consisting of: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, and -O-CH_3. In some embodiments, R^{C10d} is a linear C_1-C_5 alkyl optionally C-substituted with a single substituent selected from the group consisting of: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, and -O-CH_3.

[0339] In some embodiments of the compounds of Formula C, R^{C10d} is a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by N, S, and/or O heteroatoms. In some embodiments, R^{C10d} is a branched C_1-C_{10} alkyl, alkenyl, or alkynyl. In some embodiments, R^{C10d} is a branched C_1-C_{10} alkyl.

[0340] In some embodiments of the compounds of Formula C, R^{C10d} is $R^{C10e}R^{C10f}$. In some embodiments, R^{C10e} is a linear C_1-C_3 alkyl. In some embodiments, R^{C10f} is a 5 or 6 membered aromatic ring wherein 0-4 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-4 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen. In some embodiments, R^{C10f} is a fused bicyclic or fused tricyclic aryl group wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-6 groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl. In some embodiments, R^{C10g} is methyl. In some embodiments, each ring in the fused bicyclic or fused tricyclic aryl group independently has 4, 5 or 6 ring carbons, wherein 0-3 carbons are

independently replaced by N, S, and/or O heteroatoms; such embodiments may be substituted or unsubstituted as defined above.

[0341] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a (3-I)Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a Gly residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0342] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0343] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a (4-NH_2)Phe residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a Gly residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0344] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a (4-NO_2)Phe residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a Gly residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0345] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a hTyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a Gly residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0346] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-His residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0347] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a His residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0348] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-Ser residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0349] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-Glu residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0350] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-His residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0351] In some embodiments of the compounds of Formula A:-NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg

residue; -NH-CH(R^{5a})-C(O)- forms a (2-Ant)Ala residue; -NH-CH(R^{6a})-C(O)- forms a Gly residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0352] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue.

[0353] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{6a})-C(O)- forms a Gly residue. In some of these embodiments, -NH-CH(R^{6a})-C(O)- forms a D-Ala residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue. In some of these embodiments, -NH-CH(R^{5a})-C(O)- forms a (4-NH_2)Phe residue. In some of these embodiments, -NH-CH(R^{A1a})-C(O)- forms a Phe residue and R^{A10} is absent. In some embodiments, R^{A10} is -[linker]-R^{X}_{n1}, RA^{1e} is linear C_1-C_5 alkylenyl, and R^{A1f} is -NHC(O).

[0354] In some embodiments of the compounds of Formula A, one or more of the following conditions are met:

a) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;

b) -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

c) -NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

d) -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and/or

e) -NH-CH(R^{6a})-C(O)- forms a D-Ala residue.

[0355] In some embodiments of the compounds of Formula A, -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and -NH-CH(R^{6a})-C(O)- forms a D-Ala residue.

[0356] In some embodiments of the compounds of Formula A:-NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{6a})-C(O)- forms a Gly residue, a D-Ala residue, a D-Gln residue, or a

D-Asn residue. In some embodiments, -NH-CH(R^{A1a})-C(O)- forms a Phe residue and R^{10A} is absent. In some embodiments, R^{A10} is -[linker]-R^{X}_{n1}, R^{A1e} is linear C_1-C_5 alkylenyl, and R^{A1f} is -NH-C(O)-.

[0357] In some embodiments of the compound of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NCH_3-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue which is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr)-NH_2.

[0358] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(=NH)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue and the backbone amide is replaced with an amidine; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(=NH)-, wherein R^{5a} is a -CH_2(2-naphthyl); -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue which is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr)-NH_2.

[0359] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(=NH)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue and the backbone amide is replaced with an amidine; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some

embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(=NH)-, wherein R^{4a} is –$(CH_2)_3NHC(=NH)NH_2$; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue which is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr)-NH_2.

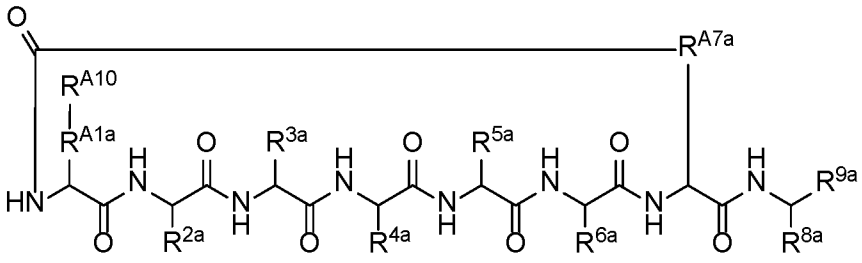
[0360] In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(=NH)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue and the backbone amide is replaced with an amidine; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments of the compounds of Formula A: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(=NH)-, wherein R^{3a} is –$(CH_2)_4NH(iPr)$; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue which is amidated. In some embodiments, -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr)-NH_2.

[0361] In some embodiments of the compounds of Formula B: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; and -NH-CH(R^{8a})-C(O)- forms a Lys(iPr) residue. In some of these embodiments, -NH-CH(R^{6a})-C(O)- forms a Gly residue, a D-Ala residue, a D-Gln residue, or a D-Asn residue; and -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue, a (2-Ant)Ala residue or a (4-NH_2)Phe residue.

[0362] In embodiments of the compounds of Formula B: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and -NH-CH(R^{6a})-C(O)- forms a D-Ala.

[0363] In some embodiments of the compounds of Formula C: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and -NH-CH(R^{6a})-C(O)- forms a D-Ala.

[0364] In some embodiments of the compound of Formula A, the compound has the structure of Formula A-I or salt or solvate thereof:



[Formula A-I]

[0365] wherein:

[0366] R^{2a} is $-(CH_2)-(R^{2b})-$(phenyl), wherein R^{2b} is absent, $-CH_2-$, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, $-N_3$, -CN, or -O-phenyl or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0367] R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{3c} is $–N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0368] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0369] R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein R^{5b} is:

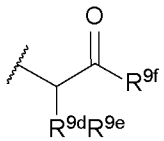
[0370] phenyl optionally substituted with one or a more of the following: 4-substituted with $-NH_2$, $-NO_2$, -OH, -SH, $-N_3$, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH;

[0371] a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$; and

[0372] wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

[0373] R^{6a} is methyl, ethyl, $-C\equiv CH$, $-CH=CH_2$, $-CH_2-R^{6b}$-OH, $-CH_2-R^{6b}$-COOH, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH_2$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0374] R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0375] R^{9a} is: $-C(O)NH_2$, $-C(O)-OH$, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, $-R^{9b}-R^{9c}$ or $-R^{9b}-$[linker]$-R^X_{n1}$; wherein R^{9b} is –C(O)NH–; and R^{9c} is , wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-CH_3$, $-N(CH_3)_2$, $-S-CH_3$, $-O-CH_3$, or phenyl, and R^{9f} is amino or –OH;

[0376] R^{A7a} is C_1-C_3 alkylenyl;

[0377] R^{A10} is absent or -[linker]$-R^X_{n1}$;

[0378] when R^{A10} is absent, then R^{A1a} is:

[0379] a linear C_1-C_5 alkyl, alkenyl, or alkynyl, wherein 0-2 carbons in C_2-C_5 are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-(CH_3)_{1-2}$, $-NH_2-CH_3$, $-N(CH_3)_{2-3}$, $-S-CH_3$, or $-O-CH_3$;

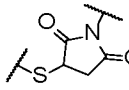
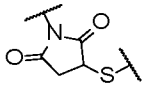
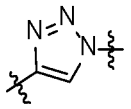
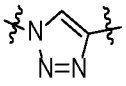
[0380] a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

[0381] $R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

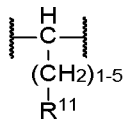
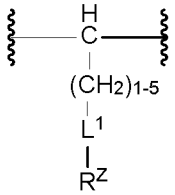
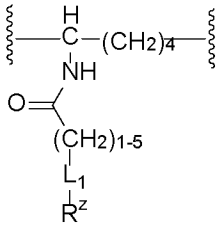
[0382] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

[0383] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, $-OR^{A1d}$, amino, $-NHR^{A1d}$, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

[0384] when R^{A10} is -[linker]$-R^X_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, alkenylenyl, or alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, $-C(O)-N(CH_3)-$, -NHC(S)-, -C(S)NH-, $-N(CH_3)C(S)-$, $-C(O)N(CH_3)-$, $-N(CH_3)C(O)-$, $-C(S)N(CH_3)-$, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, $-S(O)_2-$, $-S(O)_2-O-$, $-S(O)_2-NH-$, -S(O)-NH-, -Se-, -Se(O)-, $-Se(O)_2-$, -NHNHC(O)-, -

C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

[0385] the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

[0386] X^1 is each independently -CH_2-, , , or ;

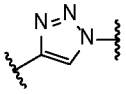
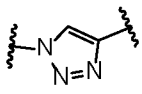
[0387] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, or –C(O)$N(CH_3)$–;

[0388] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0389] R^Z is each independently an albumin binder;

[0390] each n1 is independently 0, 1 or 2;

[0391] each R^X is an albumin binder, a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

[0392] wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

[0393] wherein 0-3 peptide backbone amides are N-methylated; and

[0394] wherein C-terminal is optionally amidated.

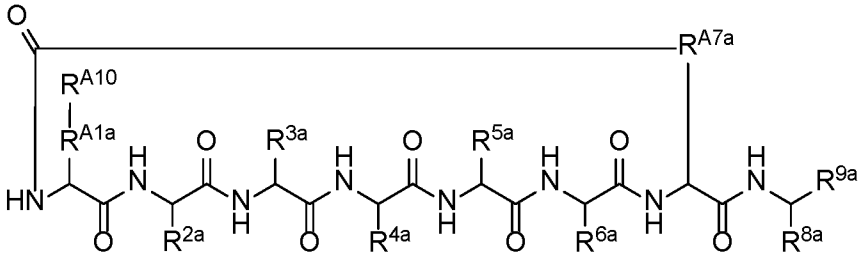
[0395] In some embodiments of the compounds of Formula A or A-I, -NH-CH(R^{A1a})-C(O)- forms an L amino acid residue.

[0396] In some embodiments of the compounds of Formula A or A-I, -NH-CH(R^{A1a})-C(O)- forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, a Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue. n some embodiments of the compounds of Formula A, -NH-CH(R^{A1a})-C(O)- forms an L-Phe residue, an L-1-Nal residue, an L-2-Nal residue, an L-Tyr residue, an L-Trp residue, an L-Lys

residue, an L-hLys residue, an L-Lys(Ac) residue, an L-Dap residue, an L-Dab residue, or an L-Orn residue.

[0397] In some embodiments of the compounds of Formula A or A-I, R^{A10} is -[linker]-R^{X}_{n1} and R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, or -CH_2-C(O)-OH.

[0398] In some embodiments of the compound of Formula A, the compound has the structure of Formula A-II or salt or solvate thereof:



[Formula A-II]

[0399] wherein:

[0400] -NH-CH(R^{2a})-C(O)- in Formula A-II forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

[0401] -NH-CH(R^{3a})-C(O)- in Formula A-II forms a Lys(iPr) residue, a Arg$(Me)_2$ (asymmetrical) residue, or a Arg(Me) residue;

[0402] -NH-CH(R^{4a})-C(O)- in Formula A-II forms a D-Arg residue or a D-hArg residue;

[0403] -NH-CH(R^{5a})-C(O)- in Formula A-II forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

[0404] -NH-CH(R^{6a})-C(O)- in Formula A-II forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

[0405] R^{8a} is $R^{8b}R^{8c}$, wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0406] R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-[linker]-R^{X}_{n1};

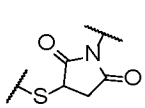
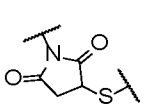
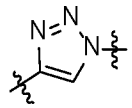
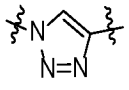
[0407] R^{9b} is –C(O)NH–;

[0408] R^{A7a} is C_1-C_3 alkylenyl;

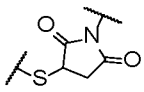
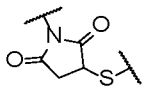
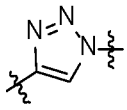
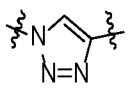
[0409] R^{A10} is absent or -[linker]-R^{X}_{n1};

[0410] when R^{A10} is absent, then R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-

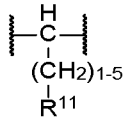
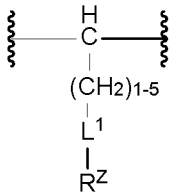
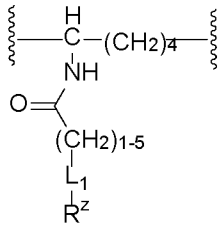
C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3, or a branched C_1-C_{10} alkyl, alkenyl, or alkynyl;

[0411] when R^{A10} is -[linker]-R^X_{n1}, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S(O)$_2$-, -S(O)$_2$-NH-, -S(O)-NH-, -NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol;the linker is each independently a linear or branched chain of 1-10 units of X^1L^1 and/or $X^1(L^1)_2$, wherein:

[0412] each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

[0413] each L^1 is independently -NH-C(O)-, -NH-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S(O)$_2$-, -S(O)$_2$-O-, -S(O)$_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -Se(O)$_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

[0414] the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

[0415] X^1 is each independently -CH_2-, , , or ;

[0416] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)C(O)$–, or –$C(O)N(CH_3)$–;

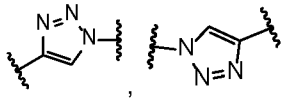
[0417] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0418] R^Z is each independently an albumin binder;

[0419] each n1 is independently 0, 1 or 2;

[0420] each R^X is an albumin binder, a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

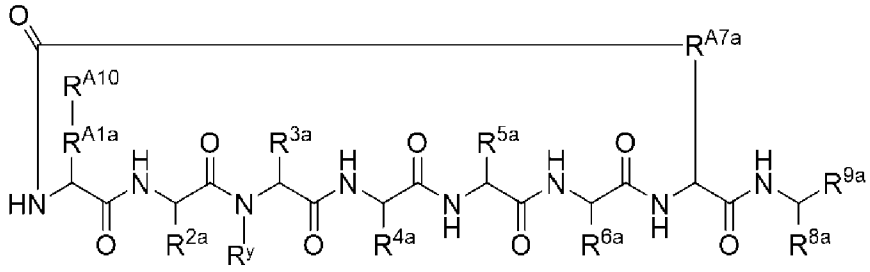
[0421] wherein 0-3 peptide backbone amides are independently replaced with

[0422]  , amidine, or thioamide;

[0423] wherein 0-3 peptide backbone amides are N-methylated; and

[0424] wherein C-terminal is optionally amidated.

[0425] In some embodiments of the compound of Formula A, the compound has the structure of Formula A-III or salt or solvate thereof:



[Formula A-III];

[0426] wherein:

[0427] R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

[0428] R^{3a} is C_1-C_5 alkyl;

[0429] R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2\text{-}3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

[0430] R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is –$N(R^{4d})_{2\text{-}3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0431] R^{5a} is -$(CH_2)_{1\text{-}3}$-R^{5b}, wherein R^{5b} is:

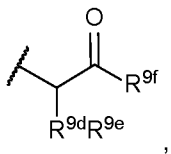
[0432] phenyl optionally substituted with one or a more of the following: 4-substituted with -NH_2, -NO_2, -OH, -SH, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH;

[0433] a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$; and

[0434] wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

[0435] R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0436] R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0437] R^{9a} is -$C(O)NH_2$, -C(O)-OH, -CH_2-$C(O)NH_2$, -CH_2-C(O)-OH, -R^{9b}-R^{9c} or -R^{9b}-[linker]-R^X_{n1}; wherein R^{9b} is –C(O)NH–; and R^{9c} is , wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-CH_3, -$N(CH_3)_2$, -S-CH_3, -O-CH_3, or phenyl, and R^{9f} is amino or –OH;

[0438] R^{A7a} is C_1-C_3 alkylenyl;

[0439] R^{A10} is absent or -[linker]-R^X_{n1};

[0440] when R^{A10} is absent, then R^{A1a} is:

[0441] a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

[0442] a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

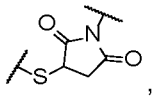
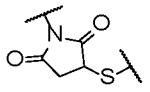
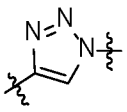
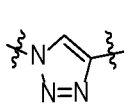
$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

[0443] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

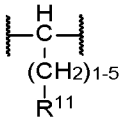
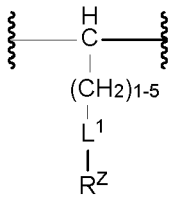
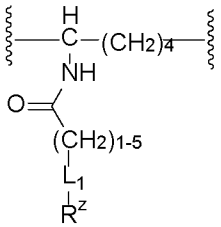
[0444] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, $-OR^{A1d}$, amino, $-NHR^{A1d}$, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

[0445] when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

[0446] R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

[0447] R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

[0448] the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

[0449] X^1 is each independently -CH_2-, , , or ;

[0450] L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)C(O)$–, or –$C(O)N(CH_3)$–;

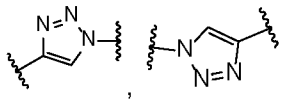
[0451] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0452] R^Z is each independently an albumin binder;

[0453] each n1 is independently 0, 1 or 2;

[0454] each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

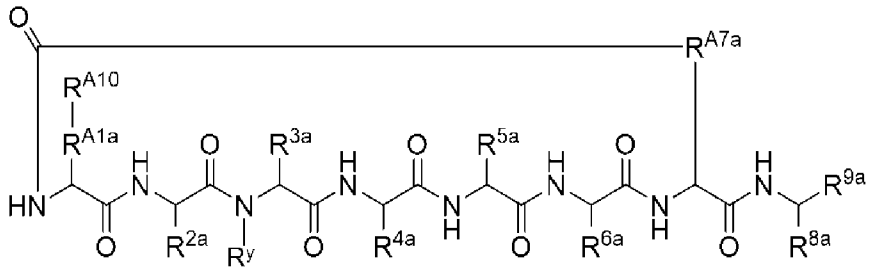
[0455] wherein 0-3 peptide backbone amides are independently replaced with

[0456]  , amidine, or thioamide;

[0457] wherein 0-3 peptide backbone amides are N-methylated; and

[0458] wherein C-terminal is optionally amidated.

[0459] In some embodiments of the compound of Formula A, the compound has the structure of Formula A-IV or salt or solvate thereof:



[Formula A-IV];

[0460] wherein:

[0461] -NH-CH(R^{2a})-C(O)- in Formula A-IV forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

[0462] -NH-CH(R^{4a})-C(O)- in Formula A-IV forms a D-Arg residue or a D-hArg residue;

[0463] -NH-CH(R^{5a})-C(O)- in Formula A-IV forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

[0464] -NH-CH(R^{6a})-C(O)- in Formula A-IV forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

[0465] R^{3a} is C_1-C_5 alkyl;

[0466] R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2\text{-}3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

[0467] R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

[0468] R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, or $-R^{9b}$-[linker]-$R^X{}_{n1}$;

[0469] R^{9b} is –C(O)NH–;

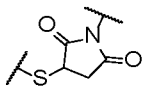
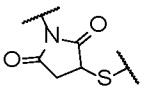
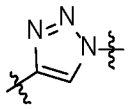
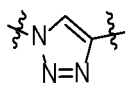
[0470] R^{A7a} is C_1-C_3 alkylenyl;

[0471] R^{A10} is absent or -[linker]-$R^X{}_{n1}$;

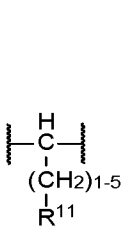
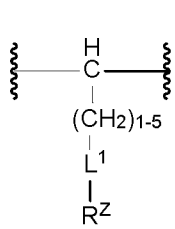
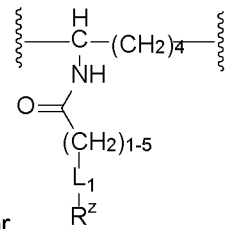
[0472] when R^{A10} is absent, then R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, $-NH_2-CH_3$, $-N(CH_3)_{2-3}$, -S-CH_3, -O-CH_3, or a branched C_1-C_{10} alkyl, alkenyl, or alkynyl;

[0473] when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

[0474] R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

[0475] R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-$N(CH_3)$-, -NHC(S)-, -C(S)NH-, -$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, $-S(O)_2$-, $-S(O)_2$-O-, $-S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, $-Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, $-OP(O)(O^-)O-$, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

[0476] the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

X^1 is each independently $-CH_2-$, , , or ;

L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, or –C(O)$N(CH_3)$–;

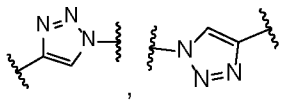
[0477] R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

[0478] R^Z is each independently an albumin binder;

[0479] each n1 is independently 0, 1 or 2;

[0480] each R^X is an albumin binder, a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

[0481] wherein 0-3 peptide backbone amides are independently replaced with

[0482]  , amidine, or thioamide;

[0483] wherein 0-3 peptide backbone amides are N-methylated; and

[0484] wherein C-terminal is optionally amidated.

[0485] In some embodiments of the compounds of Formula A, A-III, or A-IV: -NH-CH(R^{2a})-C(O)- forms a Tyr residue; -NH-CH(R^{4a})-C(O)- forms a D-Arg residue; -NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; -NH-CH(R^{6a})-C(O)- forms a D-Ala; -NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and -NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue; and wherein R^y is -$(CH_2)_4$-NH-(iPr) and R^{3a} is -CH_3.

[0486] Various embodiments discussed herein for Formula A can also apply to compounds of Formula A-I, A-II, A-III, and/or A-IV.

[0487] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, -NH-CH(R^{6a})-C(O)- forms a Gly residue, a D-Ala residue, a D-Gln residue, or a D-Asn residue.

[0488] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, -NH-CH(R^{A1a})-C(O)- forms a Phe residue and R^{A10} is absent. In some embodiments, R^{A10} is -[linker]-$R^X{}_{n1}$, R^{A1e} is linear C_1-C_5 alkylenyl, and R^{A1f} is -NH-C(O)-.

[0489] The term "[linker]" represents a linker, which may be any linker. Non-limiting examples include peptide and polyethylene glycol-based linkers.

[0490] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, each n1 in $R^X{}_{n1}$ is independently 0, 1 or 2. In some embodiments, each n1 is 0. In some embodiments, each n1 is 1. In some embodiments, each n1 is 2. In some embodiments, each n1 is the same. In some embodiments, each n1 is different.

[0491] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, each R^X is an albumin binder, a therapeutic moiety, a flurorescent label, a radiolabeled group, or a group capable of being radiolabelled. In some embodiments, each R^X is a therapeutic moiety, a flurorescent label, a radiolabeled group, or a group capable of being radiolabelled.

[0492] The present disclosure also relates to one or more of compounds comprising a compound selected from Table 2, or a salt or solvate thereof; wherein the compound is optionally bound to a radiolabeled group, a group capable of being radiolabelled, or an albumin binding group, optionally through a linker. In one embodiment, the compound of the disclosure is bound to a metal chelator and/or an albumin binder, optionally through one or more linkers.

In one embodiment, the compound of the disclosure is bound to a metal chelator and an albumin binder, optionally through one or more linkers.

[0493] The present disclosure also relates to one or more of compounds selected from Table 2, or a salt or solvate thereof; wherein the compound is optionally bound to a radiolabeled group, a group capable of being radiolabelled, or an albumin binding group, optionally through a linker. In one embodiment, the compound of the disclosure is bound to a metal chelator and/or an albumin binder, optionally through one or more linkers.In one embodiment, the compound of the disclosure is bound to a metal chelator and an albumin binder, optionally through one or more linkers.

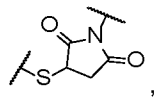
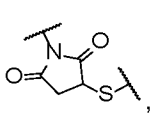
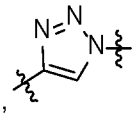
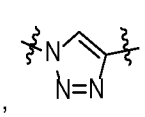
[0494] TABLE 2: Exemplary Compounds

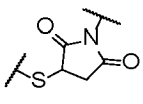
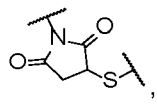
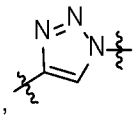
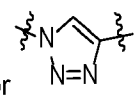
cyclo[Lys-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(ivDde)-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(ivDde)-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo(Ttn)[β-Ala(iPr)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2
cyclo(Ttn)[D-β-Ala(iPr)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2
cyclo[Lys-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(ivDde)-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(ivDde)-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(ivDde)-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys-NH_2-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2

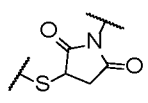
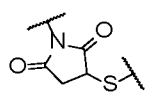
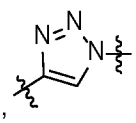
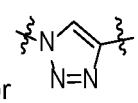
cyclo[Lys(ivDde)-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
Ψ indicates [-C(=N)-NH-] substructure *ivDde = 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-methylbutyl* *Ttn = tryptathionine*

[0495] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, each linker, if present, is independently a linear or branched chain of 1-10 units of X^1L^1, $X^1L^1X^1L^1$, $X^1L^1X^1L^1$ X^1L^1, and/or $X^1(L^1)_2$, wherein:

each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, alkenylenyl or alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

each L^1 is independently -NH-, -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol.

[0496] In some embodiments, each L^1 is independently –S–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, –C(O)N(CH_3)–, –NHC(S)–, –C(S)NH–, –N(CH_3)C(S)–, –C(S)N(CH_3)–, NHC(S)NH-, -S-, -O-, -S(O)-, -$S(O)_2$-,-Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -OP(O)(S^-)O-, , , , or .

[0497] In some embodiments, each L^1 is independently –S–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, –C(O)N(CH_3)–, , , , or .

[0498] In some embodiments, each L^1 is independently -NH-, -C(O)-, -NHC(O)-, -C(O)NH-, -N(CH_3)C(O)-, or -C(O)N(CH_3)-.

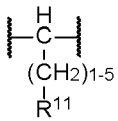
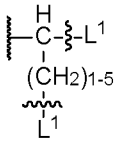
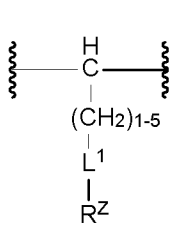
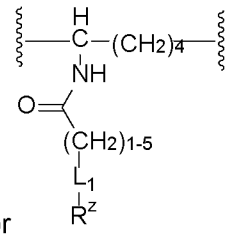
[0499] In some embodiments, linker is X^1L^1, wherein X^1 is -$(CH_2)_{1\text{-}5}$-, -CH(COOH)-$(CH_2)_{0\text{-}4}$-, or -CH($CONH_2$)-$(CH_2)_{0\text{-}4}$-; and L^1 is–NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, or –C(O)N(CH_3)–.

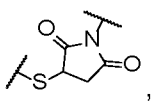
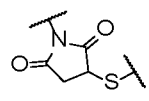
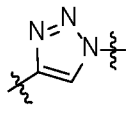
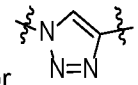
[0500] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C or Table 2, at least one linker comprises at least one carboxylic acid, sulfonic acid, sulfinic acid, or phosphoric acid, and has a net negative charge at physiological pH.

[0501] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, at least one linker comprises at least one chemical group such as a guanidino or an amino group that has a net positive charge at physiological pH.

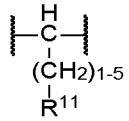
[0502] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, at least one linker consists of 1-8 units of X^1L^1 and 0-2 units of $X^1(L^1)_2$.

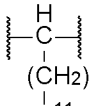
[0503] In some embodiments, each X^1 is independently a linear, branched, and/or cyclic C_1-C_{15} alkylenyl.

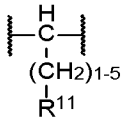
[0504] In some embodiments, each X^1 is independently: -CH_2-;  ; wherein each R^{11} is independently carboxylic acid, sulfonic acid, sulfinic acid, or phosphoric acid; ,  , or  .

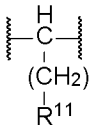
[0505] In some embodiments, each L^1 between two X^1 groups is independently –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, or –C(O)$N(CH_3)$–, and each L^1 linking an R^X is independently –S–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, –C(O)$N(CH_3)$–, , , , or  .

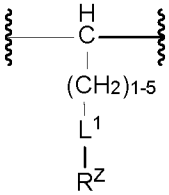
[0506] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different, and each L^1 is same or different.



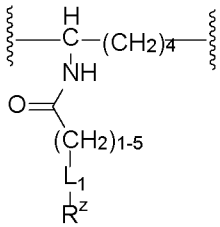
[0507] In one embodment, X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid. In one embodiment, X^1 is  , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.



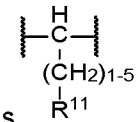
[0508] In one embodment, X^1 is , wherein each R^{11} is independently a guanidino or an amino group. In one embodiment, X^1 is  , wherein each R^{11} is independently a guanidino or an amino group.



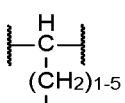
[0509] In one embodment, X^1 is , wherein each R^Z is independently an albumin binder. In some embodiments, L_1 is –NH–, –NHC(O)–, or –C(O)NH–.



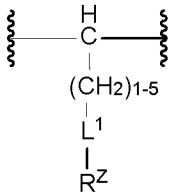
[0510] In one embodiment, X^1 is , wherein each R^Z is independently an albumin binder. In some embodiments, L_1 is –NH–, –NHC(O)–, or –C(O)NH–.



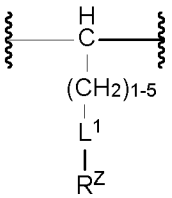
[0511] In one embodiment, the linker is X^1L^1, where X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and L^1 is –NH– or –NHC(O)–.



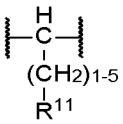
[0512] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$, where X^{1a} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; L^{1a}



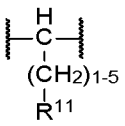
is –NH– or –NHC(O)–; X^{1b} is , wherein each R^Z is independently an albumin binder; and L^{1b} is –NH– or –NHC(O)–. In some embodiments, L_1 is –NH–, –NHC(O)–, or –C(O)NH–.



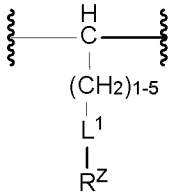
[0513] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$, where X^{1a} is , wherein



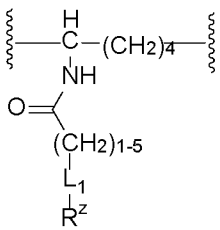
each R^Z is independently an albumin binder; L^{1a} is –NH– or –NHC(O)–; X^{1b} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and L^{1b} is –NH– or –NHC(O)–. In some embodiments, L_1 is –NH–, –NHC(O)–, or –C(O)NH–.



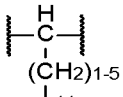
[0514] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$, where X^{1a} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; L^{1a}



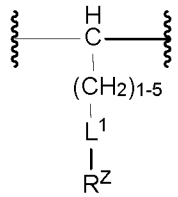
is –NH– or –NHC(O)–; X^{1b} is , wherein each R^Z is independently an albumin binder and L_1 is –NH–, –NHC(O)–, or –C(O)NH–; and L^{1b} is –NH– or –NHC(O)–.



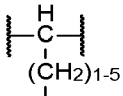
[0515] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$, where X^{1a} is , wherein each R^Z is independently an albumin binder and L_1 is –NH–,–NHC(O)–, or –C(O)NH–; L^{1a} is



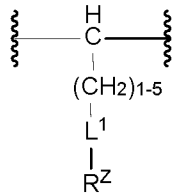
–NH– or –NHC(O)–; X^{1b} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and L^{1b} is –NH– or –NHC(O)–..



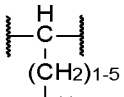
[0516] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$, where X^{1a} is , wherein each R^Z is independently an albumin binder and L_1 is –NH–, –NHC(O)–, or –C(O)NH–



; L^{1a} is –NH– or –NHC(O)–; X^{1b} is -CH_2-; L^{1b} is –NH– or –NHC(O)–; X^{1c} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and L^{1c} is –NH– or –NHC(O)–.



[0517] In one embodiment, the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$, where X^{1a} is , wherein each R^Z is independently an albumin binder and L_1 is –NH–, –NHC(O)–, or –C(O)NH–



; L^{1a} is –NH– or –NHC(O)–; X^{1b} is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; L^{1b} is –NH– or –NHC(O)–; X^{1c} is -CH_2-; and L^{1c} is –NH– or –NHC(O)–.

[0518] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein each Xaa is independently selected from a proteinogenic amino acid residue or a nonproteinogenic amino acid residue; and wherein an amino group in each Xaa is optionally methylated. In one embodment, the amino group ineach Xaa is optionally N-methylated.

[0519] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in each Xaa is optionally methylated. In one embodment, the amino group ineach Xaa is optionally N-methylated.

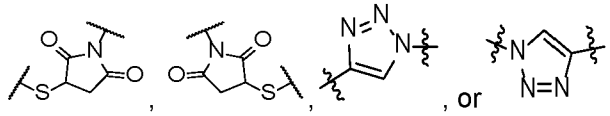
[0520] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker together with R^{A1f} forms a single amino acid residue selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in Xaa is optionally methylated. In one embodment, the amino group ineach Xaa is optionally N-methylated.

[0521] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from Dap, Dab, Orn, Arg, hArg, Agb, Agp, Acp, Pip, or N^{ε}, N^{ε}, N^{ε}-trimethyl-lysine; and wherein an amino group in each Xaa is optionally methylated. In one embodment, the amino group ineach Xaa is optionally N-methylated.

[0522] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker together with R^{A1f} forms a single amino acid residue selected from D-Arg, L-Arg, D-hArg, L-hArg, or Pip; and wherein an amino group in Xaa is optionally methylated. In one embodment, the amino group ineach Xaa is optionally N-methylated.

[0523] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, at least one linker is a linear or branched peptide of amino acid residues selected from proteinogenic amino acid residues and/or nonproteinogenic amino acid residues listed in Table 1.

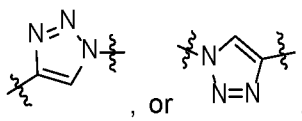
[0524] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, each L^1 between two X^1 groups in the linker is methylated or unmethylated, and wherein each L^1 linking an R^X is independently –S–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, –C(O)$N(CH_3)$–



[0525] In some embodiments, each L^1 between two X^1 groups is an unmethylated amide.

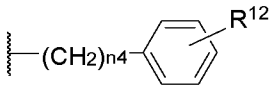
[0526] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the linker forms a peptide linker of 1 to 3 amino acids selected from one or a combination of: cysteic acid, Glu, Asp, and/or 2-aminoadipic acid (2-Aad) connected via amide bonds. In some embodiments, the linker forms a single amino acid residue selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad). In some embodiments, the linker is a cysteic acid residue.

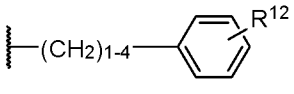
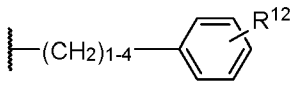
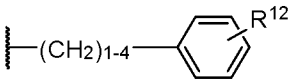
[0527] In some embodiments, each L^1 linking an R^X is independently –NHC(O)–, –C(O)NH–,

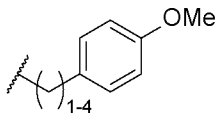
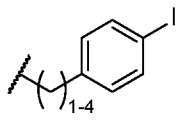


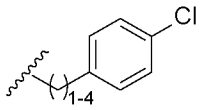
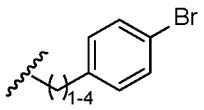
. In some embodiments, each L1 linking an R^X is independently –NHC(O)– or –C(O)NH–.

[0528] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, at least one R^X is an albumin binder. In some embodiments, the albumin binder is bonded to an

L^1 of the linker, wherein the albumin binder is: $-(CH_2)_{n2}-CH_3$ wherein n2 is 8-20; $-(CH_2)_{n3}-C(O)OH$ wherein n3 is 8-20, or  wherein n4 = 1-4 and R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3.

[0529] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, least one R^X is an albumin binder, the albumin binder is bonded to an L^1 of the linker, and the albumin binder is: $-(CH_2)_{8-20}-CH_3$, $-(CH_2)_{8-20}-C(O)OH$, or , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3. In some embodiments, the albumin binder is , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3. In some embodiments, the albumin binder is , wherein R^{12} is I, Br, Cl, H, OCH_3, NO_2 or CH_3.

[0530] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, the albumin binder is  or .

[0531] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, the albumin binder is  or .

[0532] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, at least one R^X is a radiolabeled group or a group capable of being radiolabelled (e.g. through conjugation of a radiometal or radiolabeled prosthetic group, or through an isotope-radioisotope exchange reaction).

[0533] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the compound comprises a first linker bonded to a radiolabeled group or to a group capable of being radiolabelled, and further comprises a second linker bonded to an albumin binder.

[0534] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the compound comprises a first linker bonded to a first radiolabeled group or to a first group capable of being radiolabelled, and further comprises a second linker bonded to a second radiolabeled group or to a second group capable of being radiolabelled, wherein the compound optionally further comprisies an albumin binder attached to either or both of the first linker and the second linker.

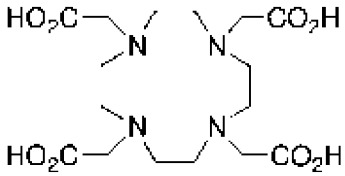
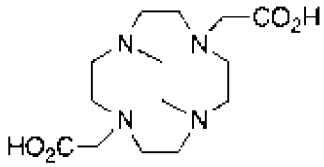
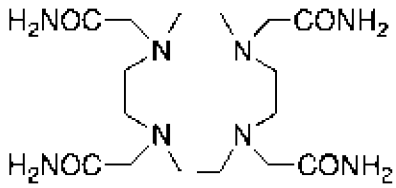
[0535] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, the compound comprises only a single linker bonded to 1-2 groups consisting of radiolabeled groups and/or group capable of being radiolabelled, the linker optionally further bonded to an albumin binder.

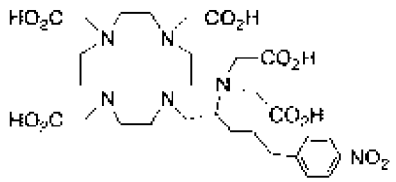
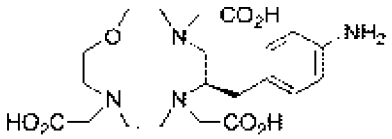
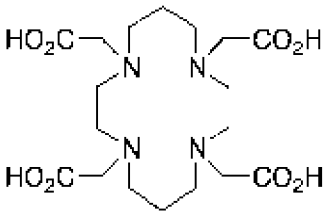
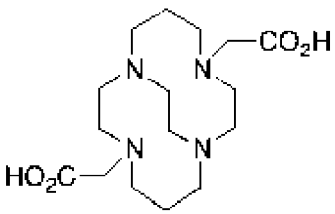
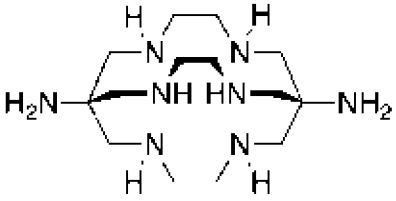
[0536] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, each group capable of being radiolabelled is independently selected from: a metal chelator optionally in complex with a radiometal or radioisotope-bound metal; a prosthetic group containing trifluoroborate (BF_3); or a prosthetic group containing a silicon-fluorine-acceptor moiety, a sulphonyl fluoride, or a phosphoryl fluoride.

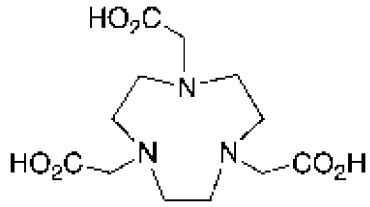
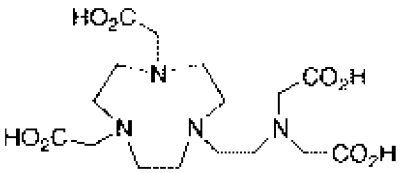
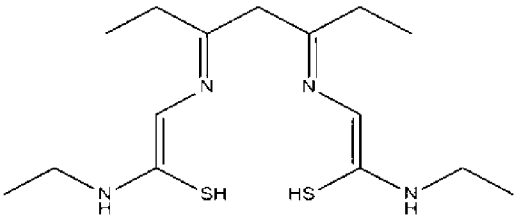
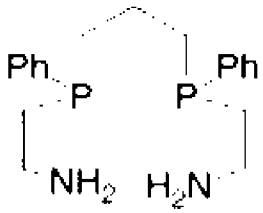
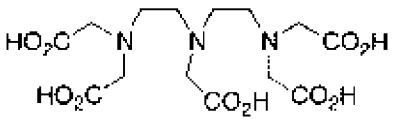
[0537] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, an R^X comprises a metal chelator optionally in complex with a radiometal (e.g. ^{68}Ga or ^{177}Lu) or in complex with a radioisotope-bound metal (e.g. $Al^{18}F$). In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2, an R^X is a metal chelator optionally in complex with a radiometal (e.g. ^{68}Ga or ^{177}Lu) or in complex with a radioisotope-bound metal (e.g. $Al^{18}F$). The chelator may be any metal chelator suitable for binding to the radiometal or to the metal-containing prosthetic group bonded to the radioisotope (e.g. polyaminocarboxylates and the like). Many suitable chelators are known, e.g. as summarized in Price and Orvig, *Chem. Soc. Rev.,* 2014, 43, 260-290, which is incorporated by reference in its entirety. Non-limiting examples of suitable chelators include those selected from the group consisting of: DOTA and derivatives; DOTAGA; NOTA; NODAGA; NODASA; CB-DO2A; 3p-C-DEPA; TCMC; DO3A; DTPA and DTPA analogues optionally selected from CHX-A"-DTPA and 1B4M-DTPA; TETA; NOPO; Me-3,2-HOPO; CB-TE1A1P; CB-TE2P; MM-TE2A; DM-TE2A; sarcophagine and sarcophagine derivatives optionally selected from SarAr, SarAr-NCS, diamSar, AmBaSar, and BaBaSar; TRAP; AAZTA; DATA and DATA derivatives; H_2-macropa or a derivative thereof; H_2dedpa, H_4octapa, H_4py4pa, H_4Pypa, H_2azapa, H_5decapa, and other picolinic acid derivatives; CP256; PCTA; C-NETA; C-NE3TA; HBED; SHBED; BCPA; CP256; YM103; desferrioxamine (DFO) and DFO derivatives; and H_6phospa. Exemplary non-limiting examples of suitable chelators and example radioisotopes (radiometals) chelated by these chelators are shown in Table 3. In alternative embodiments, an R^X comprises a chelator selected from those listed above or in Table 3, or is any other suitable chelator. One skilled in the art could replace any of the chelators listed herein with another chelator.

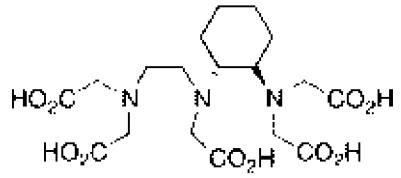
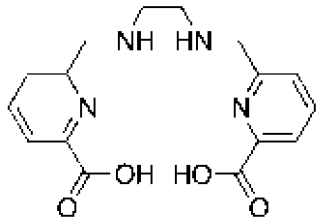
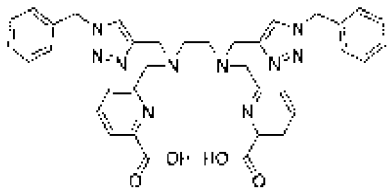
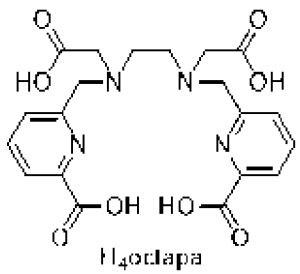
[0538] TABLE 3: Exemplary Chelators and Exemplary Isotopes Which Bind Said Chelators.

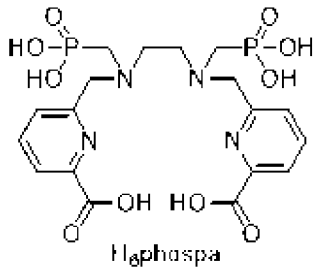
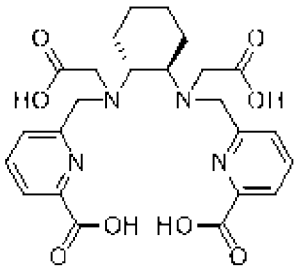
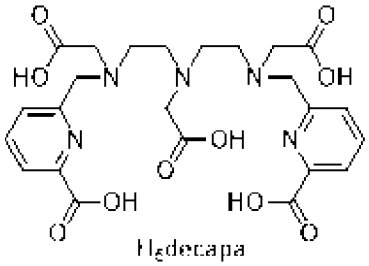
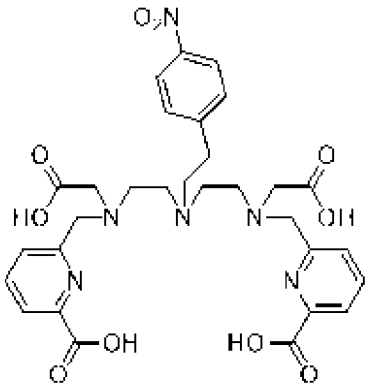
Chelator	Isotopes
	Cu-64/67 Ga-67/68

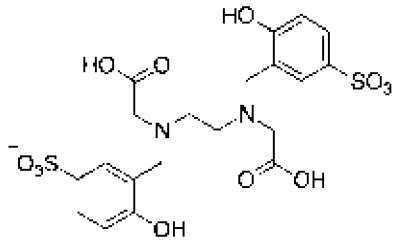
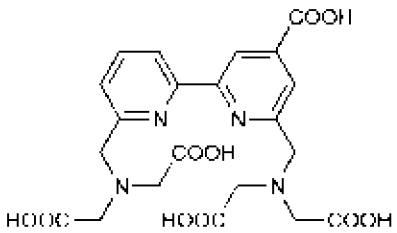
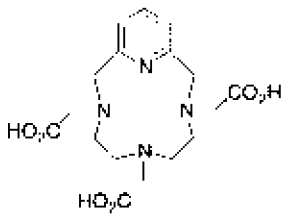
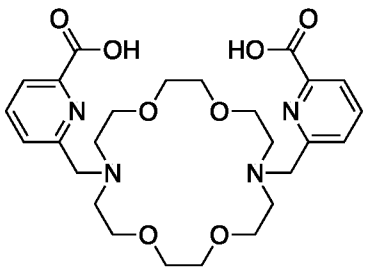
 DOTA, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid	In-111 Lu-177 Y-86/90 Bi-203/212/213 Pb-212 Ac-225 Gd-159 Yb-175 Ho-166 As-211 Sc-44/47 Pm-149 Pr-142 Sn-117m Sm-153 Tb-149/161 Er-165 Ra-223/224 Th-227
 CB-DO2A, 4,10-bis(carboxymethyl)-1,4,7,10-tetraazabicyclo[5.5.2]tetradecane	Cu-64/67
 TCMC, 1,4,7,10-tetrakis(carbamoylmethyl)-l,4,7,10-tetraazacyclododecane	Pb-212

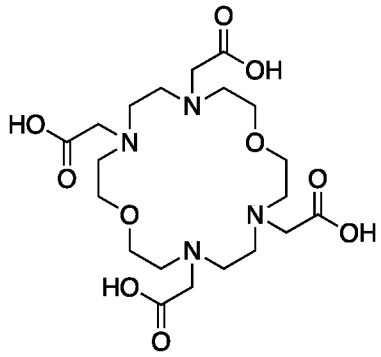
 3p-C-DEPA	Bi-212/213
 p-NH_2-Bn-Oxo-DO3A	Cu-64/67
 TETA, 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid	Cu-64/67
 CB-TE2A, 4,11-bis-(carboxymethyl)-1,4,8,11-tetraazabicyclo[6.6.2]-hexadecane	Cu-64/67
 Diamsar	Cu-64/67

 NOTA, 1,4,7-triazacyclononane-1,4,7-triacetic acid	Cu-64/67 Ga-68 In-111 Sc-44/47
 NETA, {4-[2-(bis-carboxymethylamino)-ethyl]-7-carboxymethyl-[1,4,7]triazonan-1-yl}-acetic acid	Cu-64/67 Ga-68 Lu-177 Y-86/90 Bi-213 Pb-212
 HxTSE	Au-198/199
 $P_2N_2Ph_2$	Rh-105
 DTPA, diethylenetriaminepentaacetic acid	In-111 Sc-44/47 Lu-177 Y-86/90 Sn-117m Pd-109

 CHX-A00-DTPA, 2-(p-isothiocyanatobenzyl)-Cyclohexyldiethylenetriaminepentaacetic acid	In-111 Lu-177 Y-86/90 Bi-212/213
 H_2dedpa, 1,2-[[6-(carboxy)-pyridin-2-yl]-methylamino]ethane	Cu-64/67
 H_2azapa, N,N'-[1-benzyl-1,2,3-triazole-4-yl]methyl-N,N'-[6-(carboxy)pyridin-2-yl]-1,2-diaminoethane	Cu-64/67
 H_4octapa	In-111 Lu-177 Y-86/90 Ac-225

 H_8phospa	Ac-225
 H_4*CHX*octapa	In-111 Ac-225
 H_6decapa	In-111 Lu-177 Ac-225
 H_4neunpa p Bn NO_2	In-111 Lu-177 Ac-225

 SHBED, N,N'-bis(2-hydroxy-5-sulfobenzyl)-ethylenediamine-N,N'-diacetic acid	In-111 Ga-68
 BPCA	In-111
 PCTA, 3,6,9,15-tetraazabicyclo[9.3.1]-pentadeca-1(15),11,13-triene-3,6,9,-triacetic acid	Cu-64/67
 H2-MACROPA (N,N'-bis[(6-carboxy-2-pyridil)methyl]-4,13-diaza-18-crown-6)	Ac-225

 CROWN, 2,2',2'',2'''-(1,10-dioxa-4,7,13,16-tetraazacyclooctadecane-4,7,13,16-tetrayl)tetraacetic acid	Bis-213 Lu-177 Ac-225 Tb-149/152/155/161 Th-227

[0539] It would be understood by one skilled in the art how the metal chelators, such as those listed in Table 3, can be connected to a linker or the peptide of the present disclosure by replacing one or more atoms or chemical groups of the metal chelators to form the connection. For example, one of the carboxylic acids present in the metal chelator structure can form an amide or an ester bond with the linker or the peptide. In one embodiment, the link formed between the linker and the metal chelator can be covered by the definition of the linker, such as L^1 (e.g., if an amide bond connects to the metal chelator to the linker, even if the carbonyl group could be coming from the metal chelator as drawn in Table 3, the definition of L1 (-NH-C(O)-) can encompass the amide under Formula A, A-I, A-II, A-III, A-IV, B, or C).

[0540] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, the compound excludes compounds disclosed in International Application No. PCT/CA2021/051486, which is hereby incorporated by reference in its entirety for all purposes. In some embodiments, the compound is not cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-(4-NO_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-(3-I)Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Arg(Me)$_2$(asym)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(9-Ant)Ala-Gly-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(Adamantyl)Ala-Gly-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-His-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-His-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Phe-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Leu-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Glu-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Dab-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Dap-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ser-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Gln-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-

2Nal-D-Asn-D-Glu]-Lys(iPr), cyclo[1Nal-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo[Tyr-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo[Trp-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr), cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(carboxy-m-carborane)Dap-Gly-D-Glu]-Lys(iPr), cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo[Phe-D-Tyr-Lys(iPr)-DArg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-DArg-(4-NH_2)Phe-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-DArg-hTyr-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-DArg-(COOH)Phe-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-DArg-Thyronine-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Arg(Me)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac)-Gln-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac)-Glu-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-Trp-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(D-Glu-Ac)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac-D-Arg)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac-D-Arg)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(Ac-D-Phe)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-CysAcid-CysAcid-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Glu-Ac), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Ac), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Glu-Glu-Ac), cyclo[Phe-(4NH_2)Phe-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr)-Lys(Glu-Glu-Glu-DOTA-Ga), cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Glu-Glu-Glu-DOTA-Ga), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Glu-Glu-Glu-DOTA-Ga), cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(Glu-Glu-Glu-DOTA-Ga), cyclo(tryptathionine)[Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Cys]-Lys(iPr), cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr), cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr), cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr), Cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr), cyclo[Lys($CysAcid_2$-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA-Lu)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-(4-NH_2)Phe-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-(4-NH_2)Phe-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr)-Lys(CysAcid-DOTA), cyclo[Phe-Tyr-Lys(iPr)-D-

Arg-2Nal-D-Asn-D-Glu]-Lys(iPr)-Lys(CysAcid-DOTA), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr)-Lys(CysAcid$_2$-DOTA), cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr)-Lys(CysAcid$_2$-DOTA-Ga), cyclo[Lys(CysAcid-amido-N,N-dimethyl-ammoniomethyl-trifluoroborate)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-triazole-N,N-dimethyl-ammoniomethyl-trifluoroborate)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(D-Arg-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(D-Arg-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA)-(3-I)Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Lys(CysAcid-DOTA-Ga)-(3-I)Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), cyclo[Orn(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr), or cyclo[Dap(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr).In some embodiments of the present disclosure, the compound comprises a compound from Table 4, or a salt or solvate thereof. In some embodiment, the compound is is in complex with a radioisotope.

[0541] In some embodiments of the present disclosure, the compound is selected from Table 4, or a salt or solvate thereof. In some embodiment, the compound is is in complex with a radioisotope.

[0542] In some embodiments, the compound is selected from BL34L6, BL34L7, BL34L8, BL34L11, BL34N1, BL34P1, BL34L16, BL34L20, Crown-BL34, 3NOPA-BL34L2, BL34T1, BL34L20S, Compound A, Compound B, Compound C, or Compound D, or a salt or solvate thereof. In some embodiment, the compound is is in complex with a radioisotope.

[0543] In some embodiments, the compound is selected from [^{68}Ga]Ga-BL34L6, [^{68}Ga]Ga-BL34L7, [^{177}Lu]Lu-BL34L11, [^{68}Ga]Ga-BL34L16, [^{177}Lu]Lu-BL34L20, [^{68}Ga]Ga-3NOPA-BL34L2, [^{177}Lu]Lu-crown-BL34, [^{68}Ga]Ga-BL34N1, or [^{68}Ga]Ga-BL34T1.

[0544] TABLE 4. Exemplary Compounds

cyclo[Lys(CysAcid-Lys(*p*-methoxybutyric acid)-DOTA)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr)-NH_2
cyclo[Lys(Lys(*p*-methoxybutyric acid)CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr)-NH_2
cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr)-Lys(p-methoxybutyric acid)-NH_2
cyclo[Lys(Lys(*p*-iodobutyric acid)CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr)-NH_2
cyclo[Lys(CysAcid-DOTA)-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(CysAcid-DOTA)-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2

cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2
cyclo(Ttn)[β-Ala(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2
cyclo(Ttn)[D-β-Ala(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2
Ψ indicates [-C(=N)-NH-] substructure *Ttn = tryptathionine*

[0545] In some embodiments, the compounds of the present disclosure comprise a group capable of being radiolabelled. In some embodiments, the compounds of the present disclosure comprise a metal chelator.

[0546] In some embodiments, the compounds of the present disclosure comprise DOTA as the metal chelator. In some embodiments, the compound of the present disclosure comprising DOTA as the metal chelator is in complex with a radioisotope. In one embodiment, the radioisotope is ^{64}Cu, ^{67}Cu, ^{90}Y, ^{153}Sm, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{213}Bi, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{186}Re,^{188}Re, ^{94m}Tc, ^{68}Ga, ^{61}Cu, ^{67}Ga, ^{99m}Tc, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{117m}Sn, ^{165}Er, ^{211}At, ^{203}Pb, ^{212}Pb, ^{47}Sc, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, or ^{114m}In. In one embodiment, the radioisotope is ^{177}Lu, ^{111}In, ^{213}Bi, ^{68}Ga, ^{67}Ga, ^{203}Pb, ^{212}Pb, ^{44}Sc, ^{47}Sc, ^{90}Y, ^{86}Y, ^{225}Ac, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb, ^{165}Er, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{64}Cu, or ^{67}Cu. In one embodiment, the radioisotope in complex with DOTA is ^{68}Ga or ^{67}Ga.

[0547] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X of the compound is a polyaminocarboxylate chelator. In some such embodiments, the chelator is attached through an amide bond. In some embodiments, R^X is: DOTA or a derivative thereof; TETA or a derivative thereof; SarAr or a derivative thereof; NOTA or a derivative thereof; TRAP or a derivative thereof; HBED or a derivative thereof; 2,3-HOPO or a derivative thereof; PCTA (3,6,9,15-tetraazabicyclo[9.3.1]-pentadeca-1(15),11,13-triene-3,6,9,-triacetic acid) or a derivative thereof; DFO or a derivative thereof; DTPA or a derivative thereof; OCTAPA (N,N'-bis(6-carboxy-2-pyridylmethyl)-ethylenediamine-N,N'-diacetic acid) or a derivative thereof; or H2-MACROPA or a derivative thereof. In some embodiments, an R^X is DOTA. In some embodiments, an R^X is a chelator moiety in complex with radioisotope X wherein X is ^{64}Cu, ^{67}Cu, ^{90}Y, ^{111}In, ^{114m}In, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{213}Bi, ^{224}Ra, ^{212}Bi, ^{212}Pb, ^{227}Th, ^{223}Ra, ^{47}Sc, ^{186}Re or ^{188}Re. In some embodiments, X is ^{177}Lu. In some embodiments, an R^X is a chelator moiety in complex with radioisotope X wherein X is ^{64}Cu, ^{68}Ga, ^{86}Y, ^{111}In, ^{94m}Tc, ^{44}Sc, ^{89}Zr, or ^{99m}Tc. In some embodiments, X is ^{68}Ga.

[0548] In some embodiments, the chelator is conjugated with a radioisotope. The conjugated radioisotope may be, without limitation, ^{68}Ga, ^{61}Cu, ^{64}Cu, ^{67}Ga, ^{99m}Tc, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr,

^{90}Nb, ^{177}Lu, ^{117m}Sn, ^{165}Er, ^{90}Y, ^{227}Th, ^{225}Ac, ^{213}Bi, ^{212}Bi, ^{211}At, ^{203}Pb, ^{212}Pb, ^{47}Sc, ^{166}Ho, ^{188}Re, ^{186}Re, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{114m}In, and the like. In some embodiments, the chelator is a chelator from Table 3 and the conjugated radioisotope is a radioisotope indicated in Table 3 as a binder of the chelator.

[0549] In some embodiments, the chelator is not conjugated to a radioisotope.

[0550] In some embodiments, the chelator is: DOTA or a derivative thereof, conjugated with ^{177}Lu, ^{111}In, ^{213}Bi, ^{68}Ga, ^{67}Ga, ^{203}Pb, ^{212}Pb, ^{44}Sc, ^{47}Sc, ^{90}Y, ^{86}Y, ^{225}Ac, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb, ^{165}Er, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{64}Cu or ^{67}Cu; H2-MACROPA conjugated with ^{225}Ac; Me-3,2-HOPO conjugated with ^{227}Th; H_4py4pa conjugated with ^{225}Ac, ^{227}Th or ^{177}Lu; H_4pypa conjugated with ^{177}Lu; NODAGA conjugated with ^{68}Ga; DTPA conjugated with ^{111}In; or DFO conjugated with ^{89}Zr.

[0551] In some embodiments, the chelator is TETA, SarAr, NOTA, TRAP, HBED, 2,3-HOPO, PCTA, DFO, DTPA, OCTAPA or another picolinic acid derivative.

[0552] In some embodiments, the compounds of the present disclosure comprise CROWN as the metal chelator. In some embodiments, the compound of the present disclosure comprising CROWN as the metal chelator is in complex with a radioisotope. In some embodiments, the radioisotope is ^{225}Ac. In some embodiments, the radioisotope is ^{227}Th. In some embodiments, the radioisotope is ^{152}Tb, ^{155}Tb, ^{149}Tb, or ^{161}Tb.

[0553] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a chelator for radiolabelling with ^{99m}Tc, ^{94m}Tc, ^{186}Re, or ^{188}Re, such as mercaptoacetyl, hydrazinonicotinamide, dimercaptosuccinic acid, 1,2-ethylenediylbis-L-cysteine diethyl ester, methylenediphosphonate, hexamethylpropyleneamineoxime and hexakis(methoxy isobutyl isonitrile), and the like. In some embodiments, an R^X is a chelator, wherein the chelator is mercaptoacetyl, hydrazinonicotinamide, dimercaptosuccinic acid, 1,2-ethylenediylbis-L-cysteine diethyl ester, methylenediphosphonate, hexamethylpropyleneamineoxime or hexakis(methoxy isobutyl isonitrile). In some of these embodiments, the chelator is bound by a radioisotope. In some such embodiments, the radioisotope is ^{99m}Tc, ^{94m}Tc, ^{186}Re, or ^{188}Re.

[0554] In one embodiment of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, Table 2 or derivatives thereof (e.g., where compounds of Table 2 is bound to a radiolabeled group or a group capable of being radiolabelled, optionally through a linker), or Table 4, the radioisotope is ^{64}Cu, ^{67}Cu, ^{90}Y, ^{153}Sm, ^{152}Tb, ^{155}Tb, ^{149}Tb, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{213}Bi, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{186}Re, ^{188}Re, ^{94m}Tc, ^{68}Ga, ^{61}Cu, ^{67}Ga, ^{99m}Tc, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{117m}Sn, ^{165}Er, ^{211}At, ^{203}Pb, ^{212}Pb, ^{47}Sc, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, or ^{114m}In. In one embodiment, the radioisotope is ^{177}Lu, ^{111}In, ^{213}Bi, ^{68}Ga, ^{67}Ga, ^{203}Pb, ^{212}Pb, ^{44}Sc, ^{47}Sc, ^{90}Y, ^{86}Y, ^{225}Ac, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb, ^{165}Er, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{64}Cu, or ^{67}Cu.

[0555] In one embodiment of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope, the compound is bound to a metal chelator complexed with an imaging radioisotope, or the compound is bound to a prosthetic group containing BF_3 comprising an imaging radioisotope.

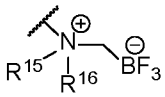
[0556] In one embodiment of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I, ^{152}Tb, ^{155}Tb, or ^{72}As. In one embodiment, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{131}I, ^{123}I, ^{124}I or ^{72}As.

[0557] In one embodiment of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, at least one R^X comprises an imaging radioisotope or is complexed with a therapeutic radioisotope, or the compound is bound to a metal chelator complexed with a therapeutic radioisotope.

[0558] In one embodiment of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, the therapeutic radioisotope is ^{165}Er, ^{212}Bi, ^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu, ^{111}In, ^{213}Bi, ^{212}Pb, ^{47}Sc, ^{90}Y, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac, ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu, or ^{67}Cu.

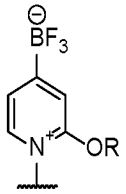
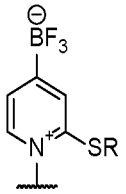
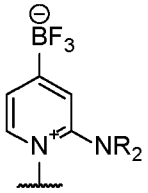
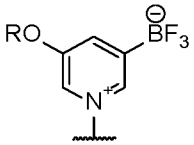
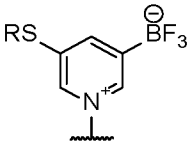
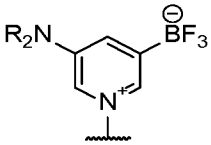
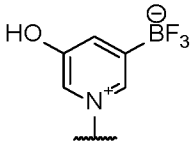
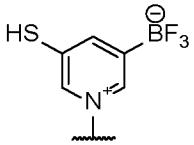
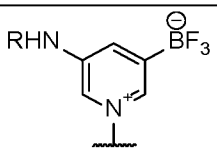
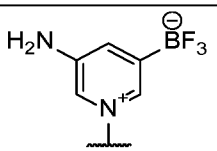
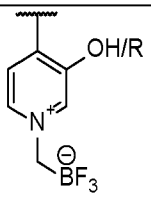
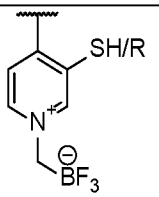
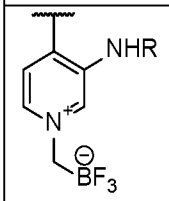
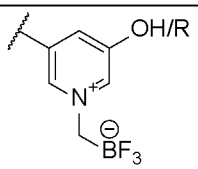
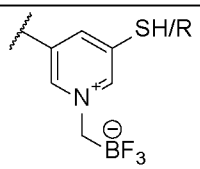
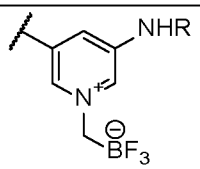
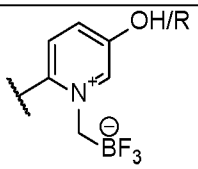
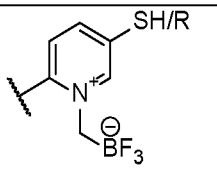
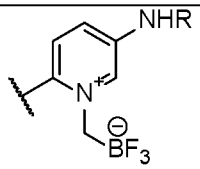
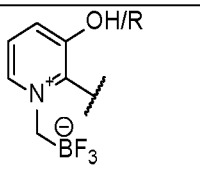
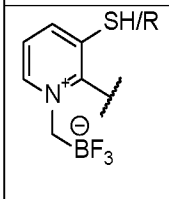
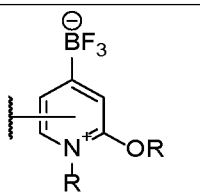
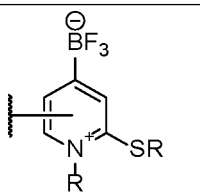
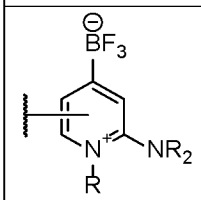
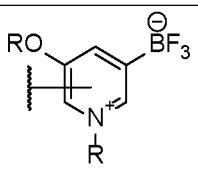
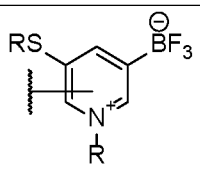
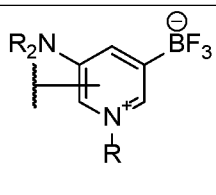
[0559] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a chelator that can bind ^{18}F-aluminum fluoride ($[^{18}F]AlF$), such as 1,4,7-triazacyclononane-1,4-diacetate (NODA) and the like. In some embodiments, the chelator is NODA. In some embodiments, the chelator is bound by $[^{18}F]AlF$.

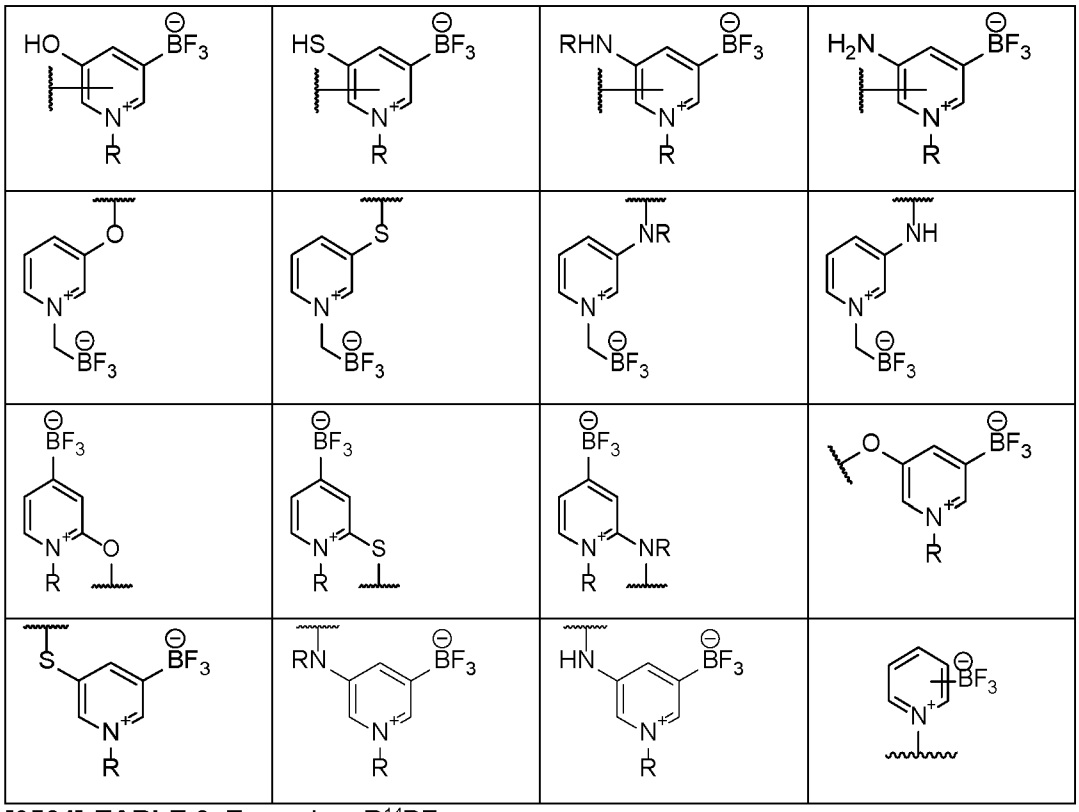
[0560] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a chelator that can bind ^{72}As or ^{77}As, such as a trithiol chelate and the like. In some embodiments, the chelator is a trithiol chelate. In some embodiments, the chelator is conjugated to ^{72}As. In some embodiments, the chelator is conjugated to ^{77}As.

[0561] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a prosthetic group containing a trifluoroborate (BF_3), capable of $^{18}F/^{19}F$ exchange radiolabeling. Such an R^X group may be the only R^X (n1 = 1), or may be in addition to additional R^X groups, which may be the same as or different than the first R^X. The prosthetic group may be $-R^{13}R^{14}BF_3$, wherein R^{13} is independently $–(CH_2)_{1\text{-}5}–$ and the group $–R^{14}BF_3$ may independently be selected from one or a combination of those listed in Table 5 (below), Table 6 (below), or  wherein each R^{15} and each R^{16} are independently C_1-C_5 linear or branched alkyl groups. For Tables 5 and 6, the R in the pyridine substituted with –OR, –SR, –NR–, –NHR or $–NR_2$ groups is C_1-C_5 branched or linear alkyl.

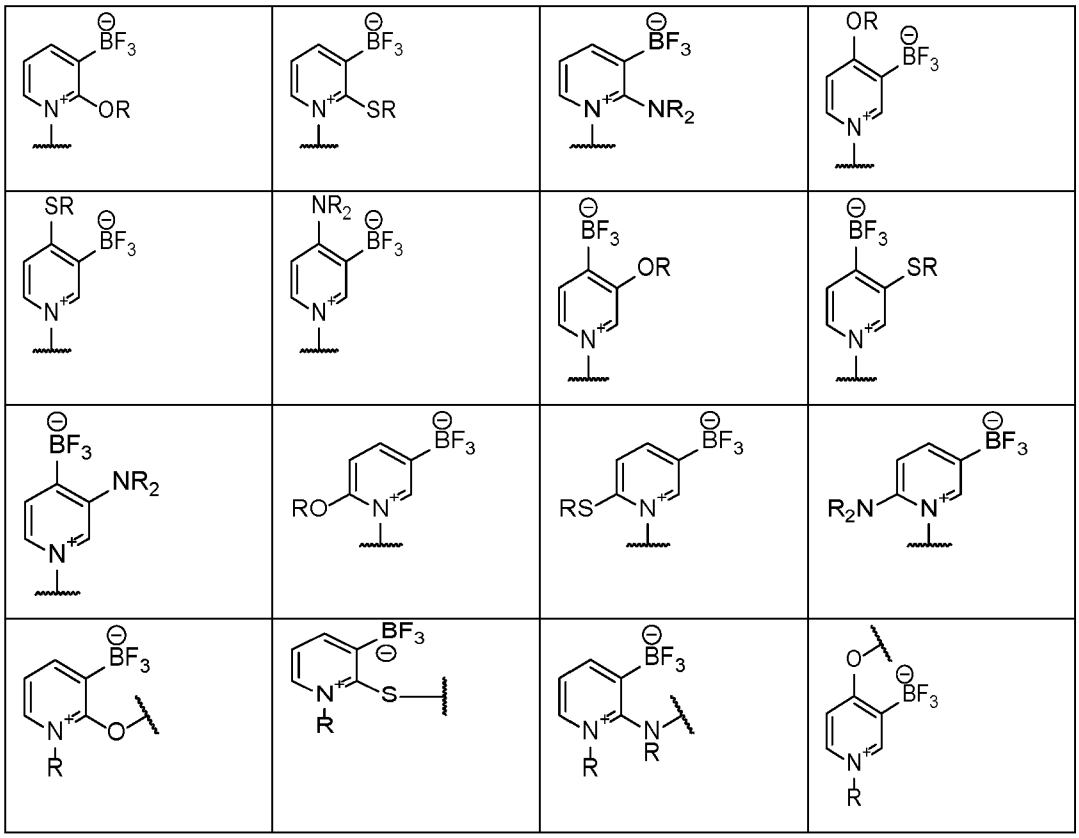
[0562] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, -$R^{14}BF_3$ is selected from those listed in Table 5. In some embodiments, -$R^{14}BF_3$ is independently selected from one or a combination of those listed in Table 6. In some embodiments, at least one fluorine is ^{18}F. In some embodiments, all three fluorines are ^{19}F.

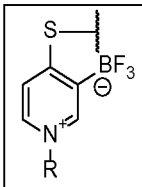
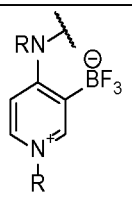
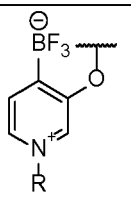
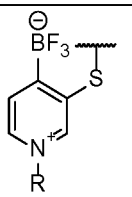
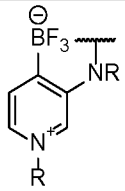
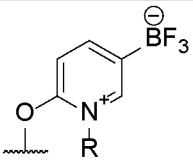
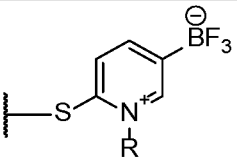
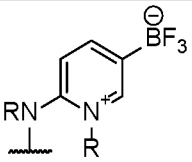
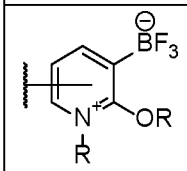
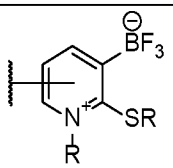
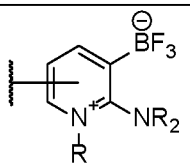
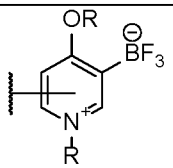
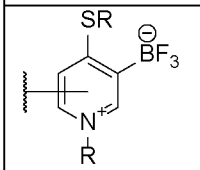
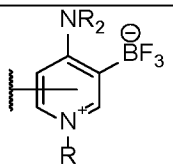
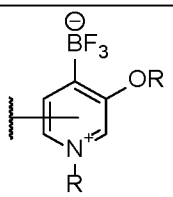
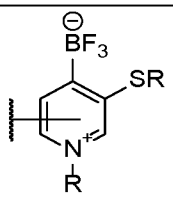
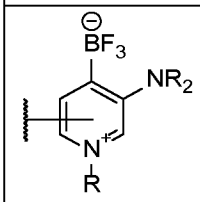
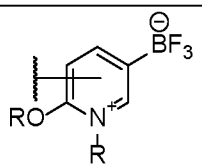
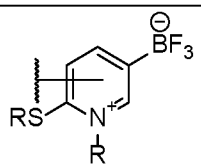
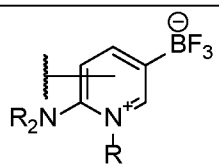
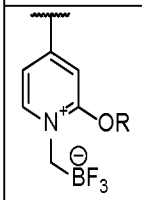
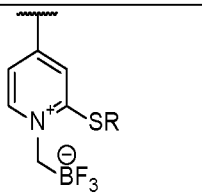
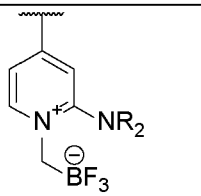
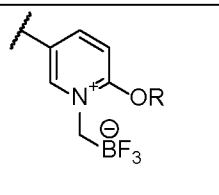
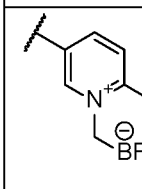
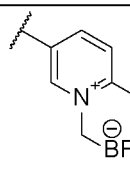
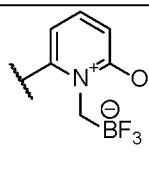
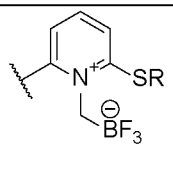
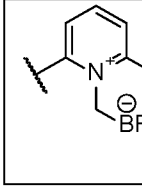
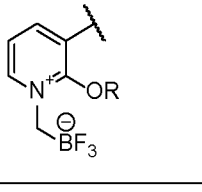
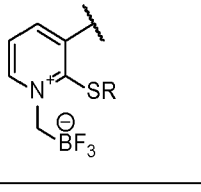
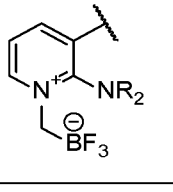
[0563] TABLE 5. Exemplary $R^{14}BF_3$ groups.

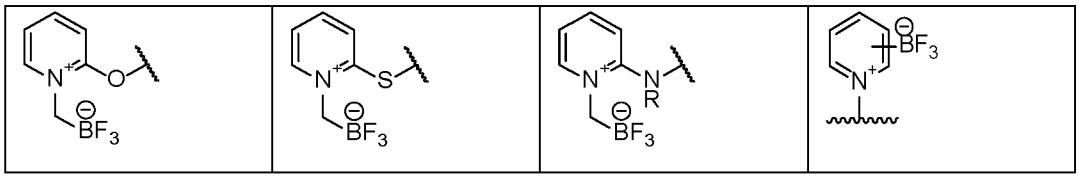
			
			
			
			
			
			
			

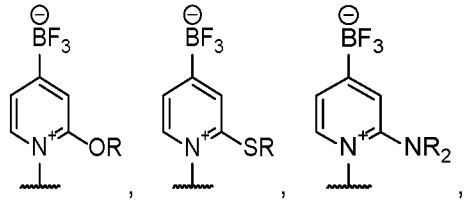
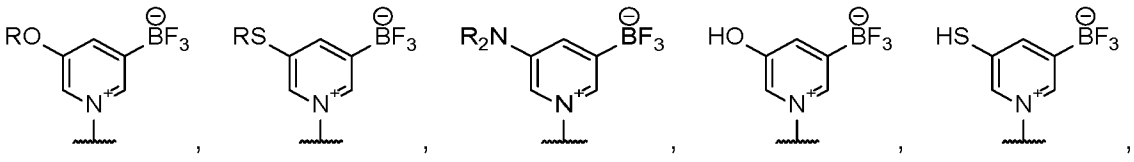
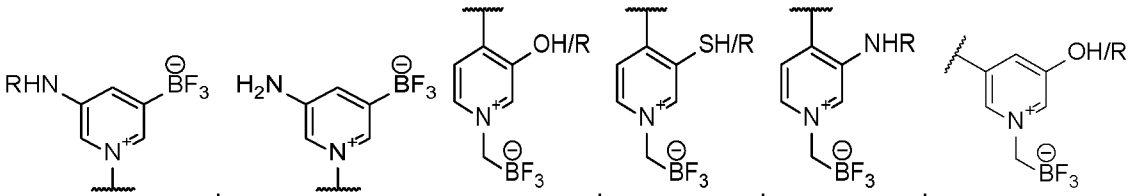
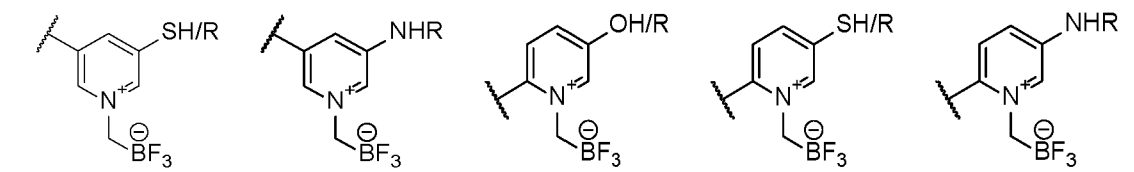
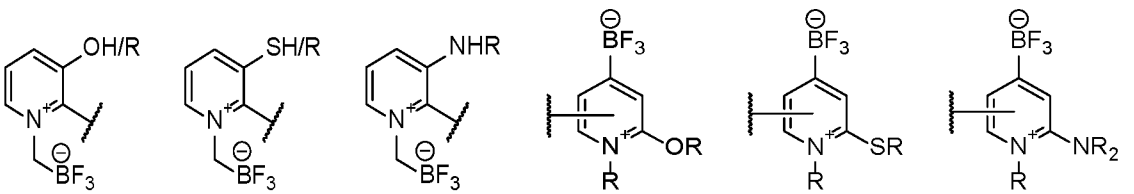
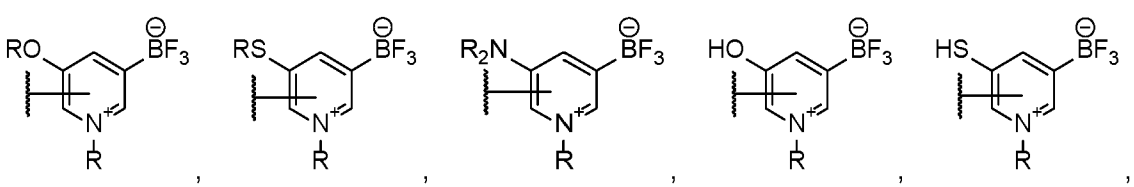
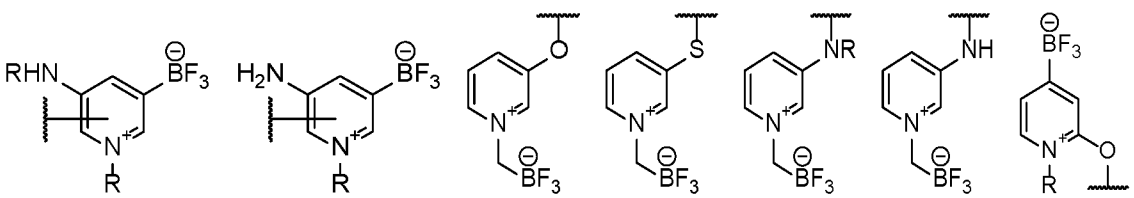


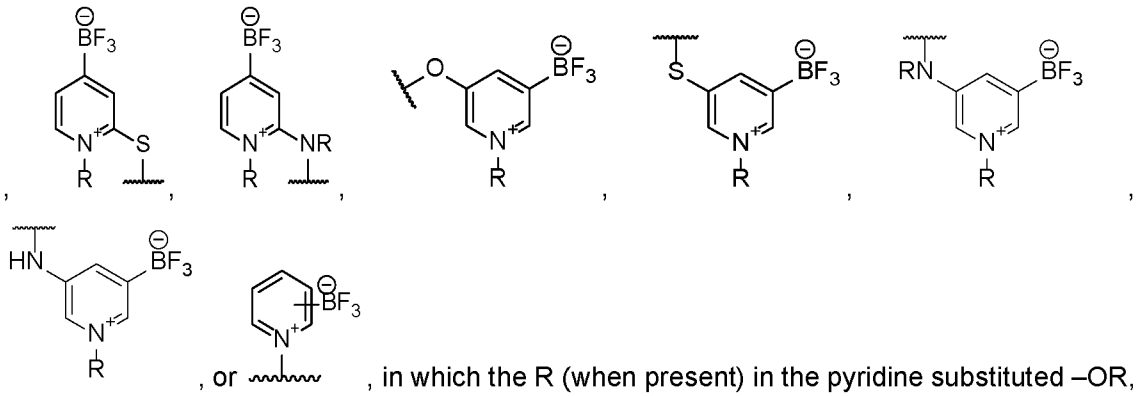
[0564] TABLE 6. Exemplary $R^{14}BF_3$ groups.



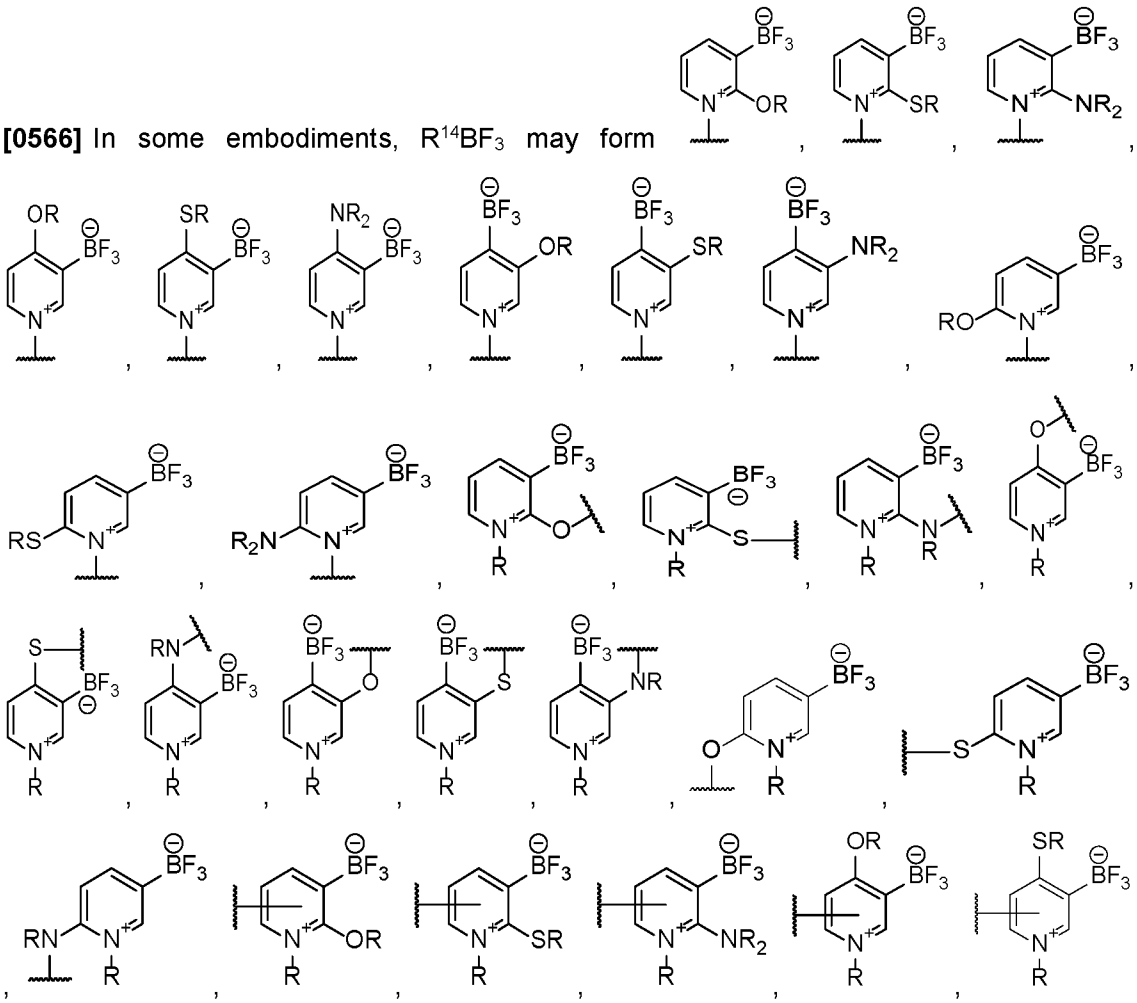


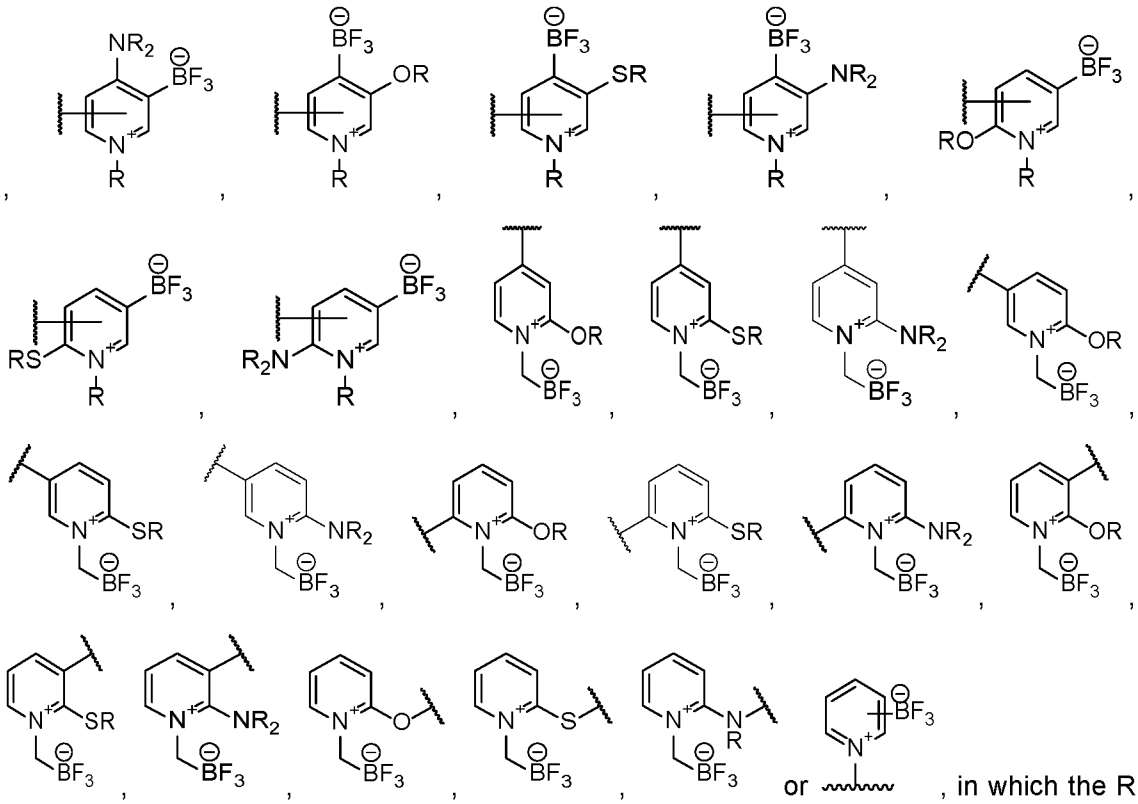
[0565] In some embodiments, $R^{14}BF_3$ may form , , , , , , .

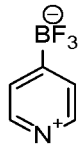


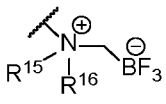
, in which the R (when present) in the pyridine substituted –OR, –SR, –NR–, –NHR or –NR_2 is a branched or linear C_1-C_5 alkyl. In some embodiments, R is a branched or linear C_1-C_5 saturated alkyl. In some embodiments, R is methyl. In some embodiments, R is ethyl. In some embodiments, R is propyl. In some embodiments, R is isopropyl. In some embodiments, R is n-butyl. In some embodiments, one fluorine is ^{18}F. In some embodiments, all three fluorines are ^{19}F.

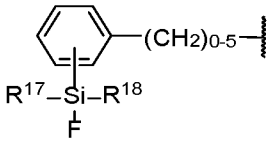
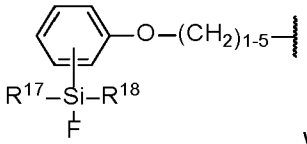
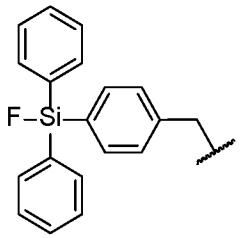
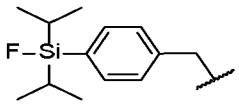
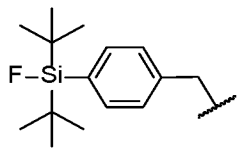
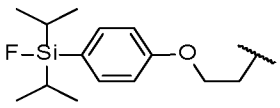
[0566] In some embodiments, $R^{14}BF_3$ may form

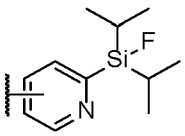
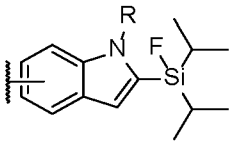
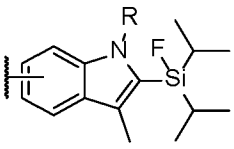




(when present) in the pyridine substituted –OR, –SR, –NR– or –NR_2 is branched or linear C_1-C_5 alkyl. In some embodiments, R is a branched or linear C_1-C_5 saturated alkyl. In some embodiments, R is methyl. In some embodiments, R is ethyl. In some embodiments, R is propyl. In some embodiments, R is isopropyl. In some embodiments, R is n-butyl. In some embodiments, -$R^{14}BF_3$ is . In some embodiments, one fluorine is ^{18}F. In some embodiments, all three fluorines are ^{19}F.

[0567] In some embodiments, -$R^{14}BF_3$ is . In some embodiments, R^{15} is methyl. In some embodiments, R^{15} is ethyl. In some embodiments, R^{15} is propyl. In some embodiments, R^{15} is isopropyl. In some embodiments, R^{15} is butyl. In some embodiments, R^{15} is n-butyl. In some embodiments, R^{15} is pentyl. In some embodiments, R^{16} is methyl. In some embodiments, R^{16} is ethyl. In some embodiments, R^{16} is propyl. In some embodiments, R^{16} is isopropyl. In some embodiments, R^{16} is butyl. In some embodiments, R^{16} is n-butyl. In some embodiments, R^{16} is pentyl. In some embodiments, R^{15} and R^{16} are both methyl. In some embodiments, at least one fluorine is ^{18}F. In some embodiments, all three fluorines are ^{19}F.

[0568] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a prosthetic group containing a silicon-fluorine-acceptor moiety. In some embodiments, the fluorine of the silicon-fluorine acceptor moiety is ^{18}F. The prosthetic groups containing a silicon-fluorine-acceptor moiety may be independently selected from one or a combination of the following:  or  wherein R^{17} and R^{18} are independently a linear or branched, cyclic or acyclic, and/or aromatic or non-aromatic C_1-C_{10} alkyl, alkenyl or alkynyl group. In some embodiments, R^{17} and R^{18} are independently selected from the group consisting of phenyl, tert-butyl, sec-propyl, isopropyl, methyl, pyridyl, 2-indolyl, and 3-indolyl. In some embodiments, the prosthetic group is . In some embodiments, the prosthetic group is . In some embodiments, the prosthetic group is . In some embodiments, the prosthetic group is . In some embodiments, the prosthetic group is a heteroarylated exemplified by the following abut not limited to:

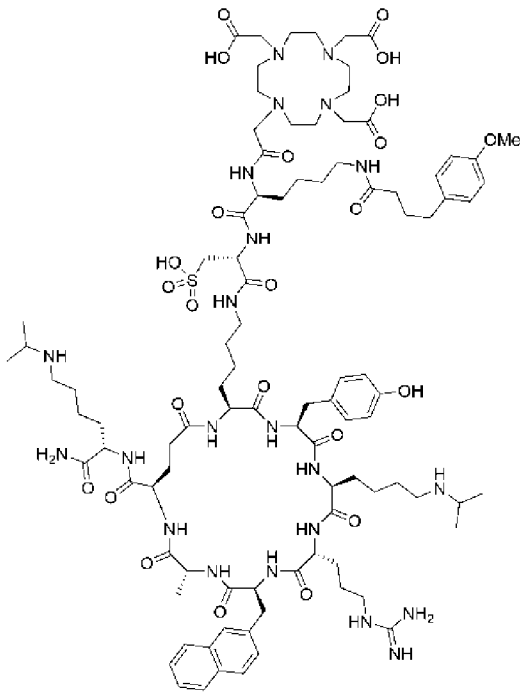
  , wherein R is hydrogen, alkyl, or aryl.

[0569] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, an R^X is a therapeutic moiety, including any chemical moiety capable of producing a therapeutic effect, e.g. small molecule drugs.

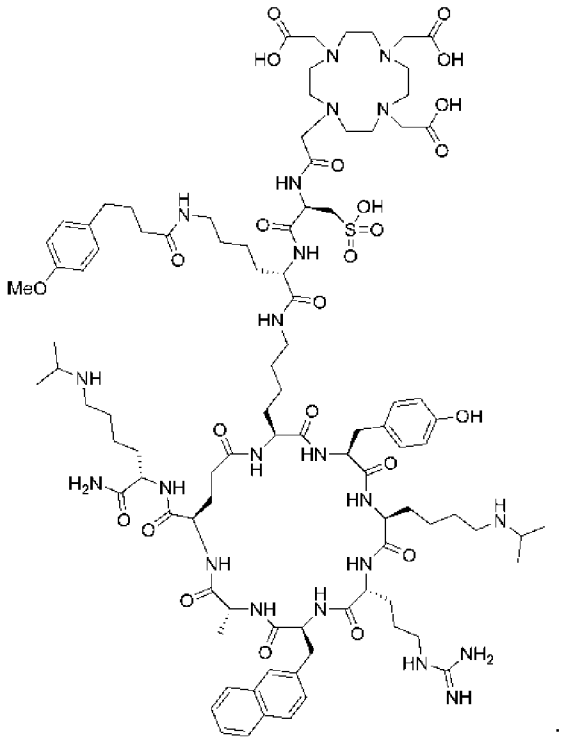
[0570] In some embodiments of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, R^X is fluorescent label.

[0571] The present disclosure also relates to a composition comprising any one of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4 as described herein.

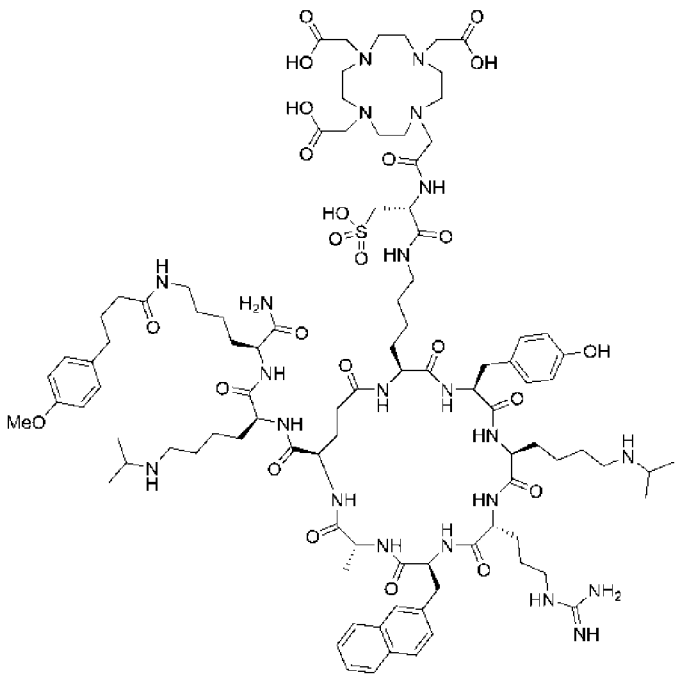
[0572] In some embodiments of the compounds of Formula A, the compound is:



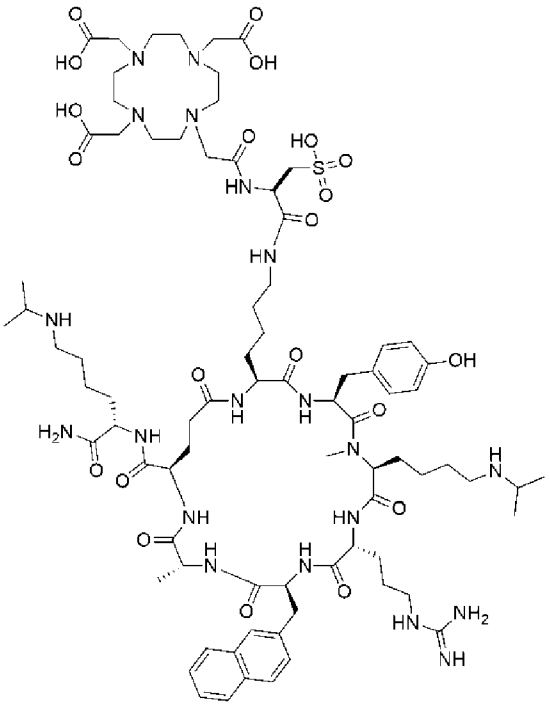
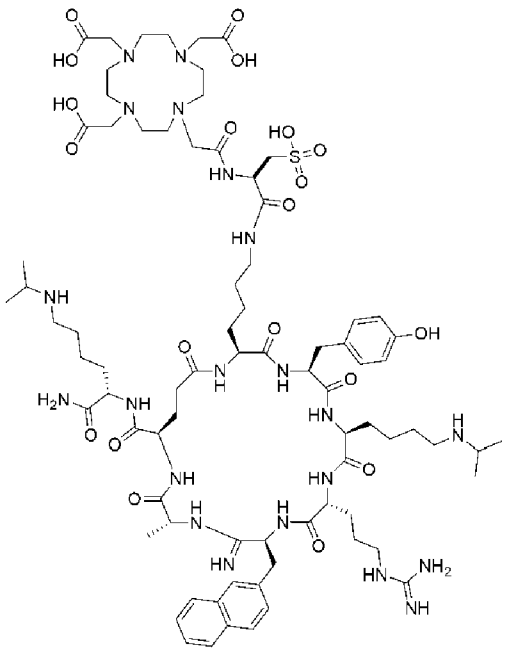
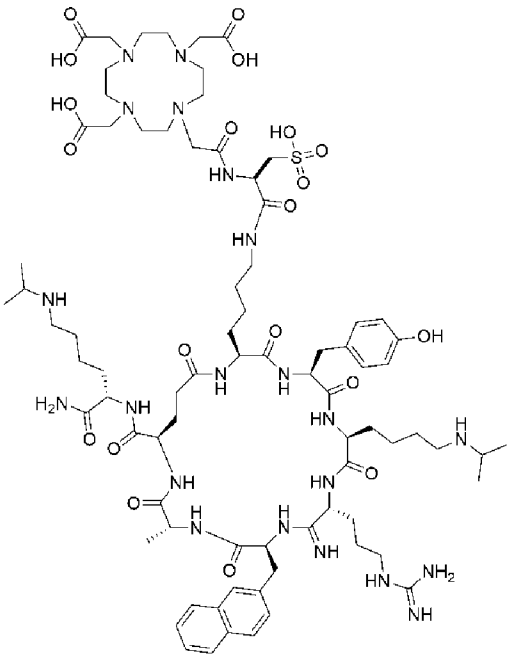
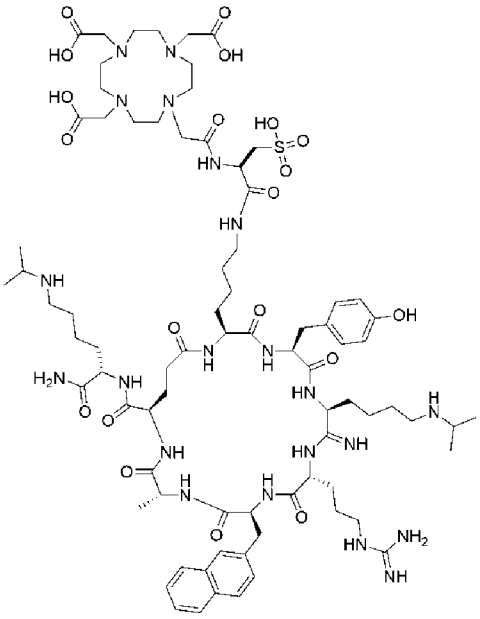
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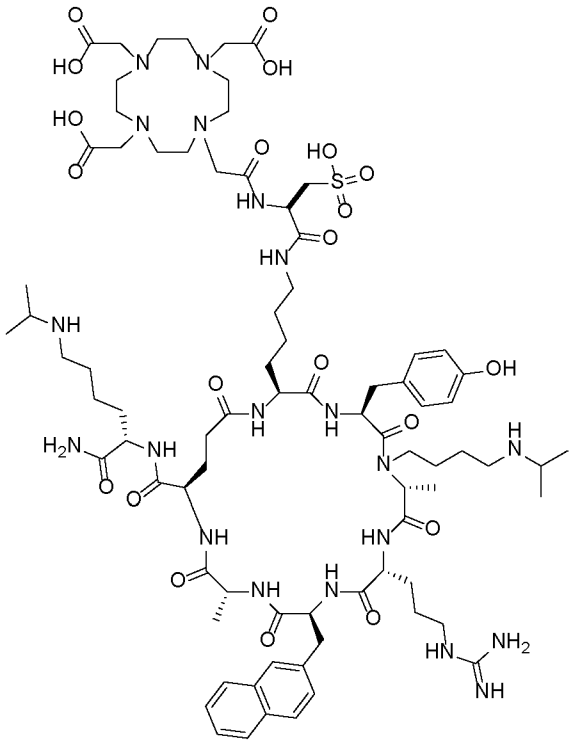


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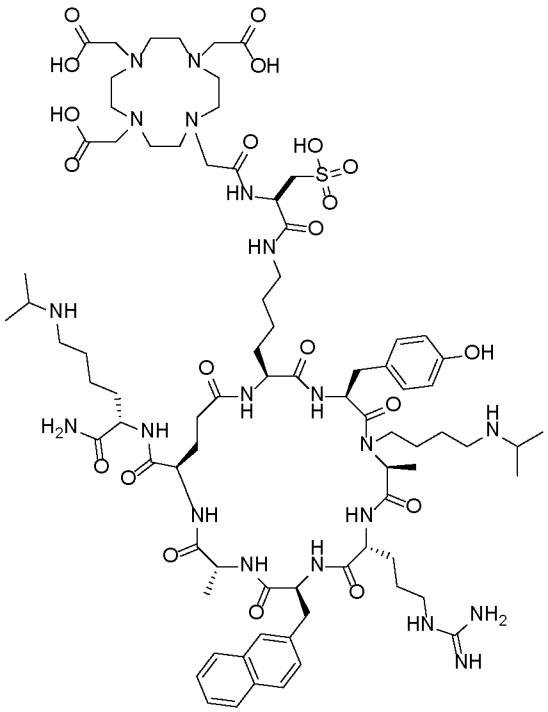


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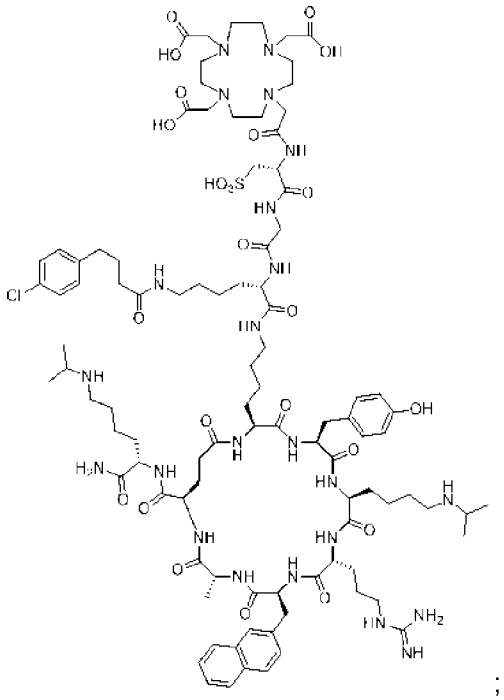

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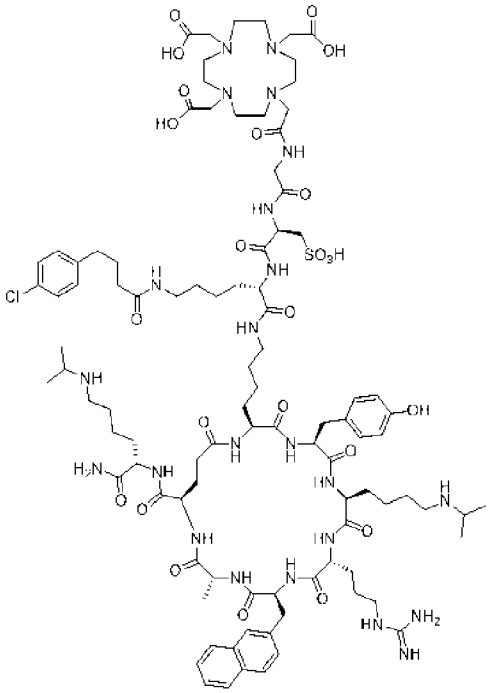
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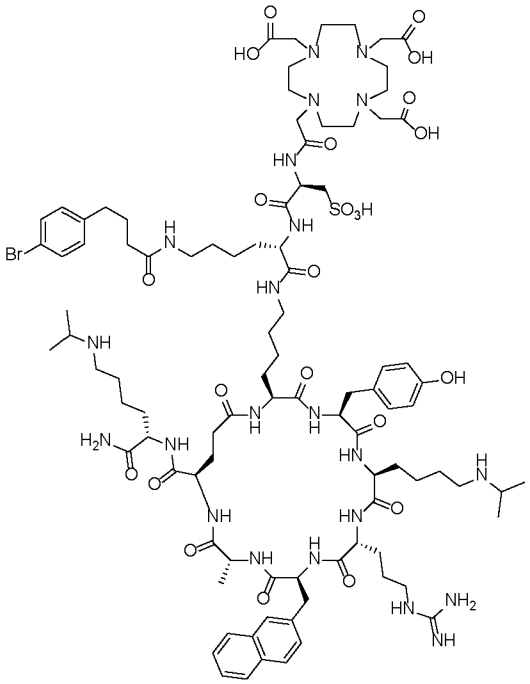


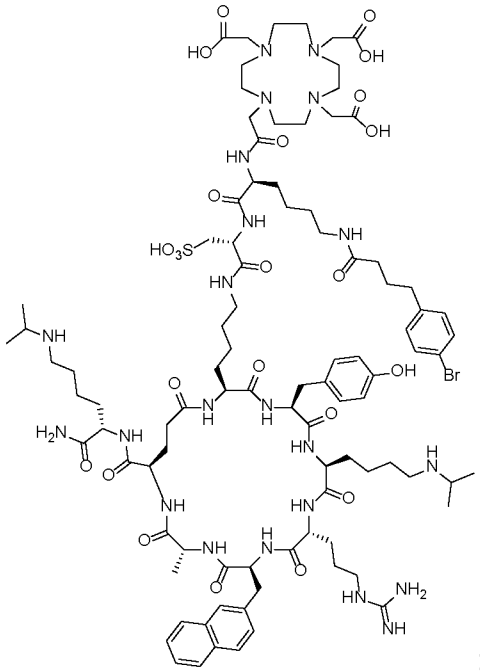
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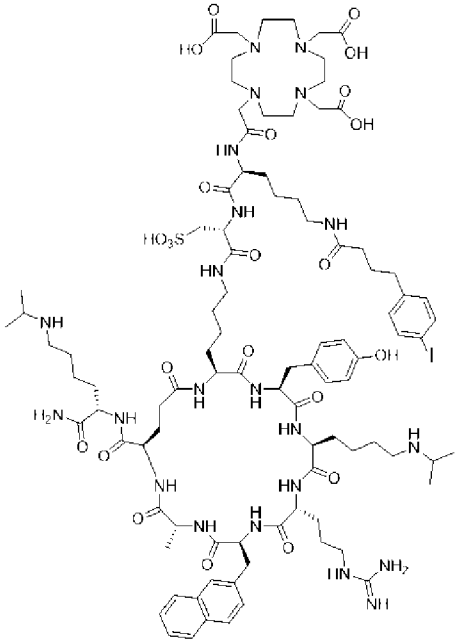


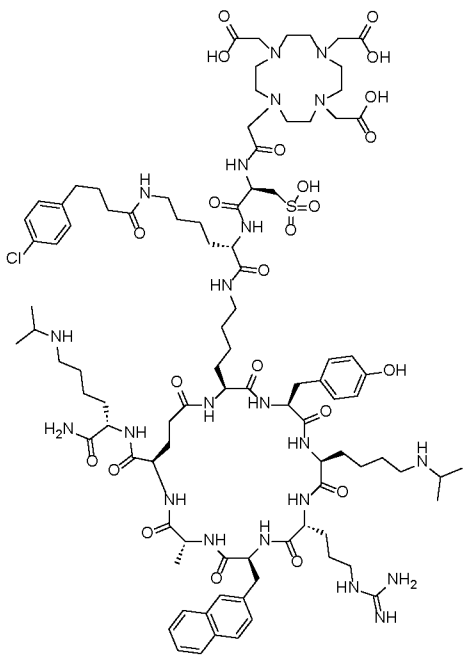
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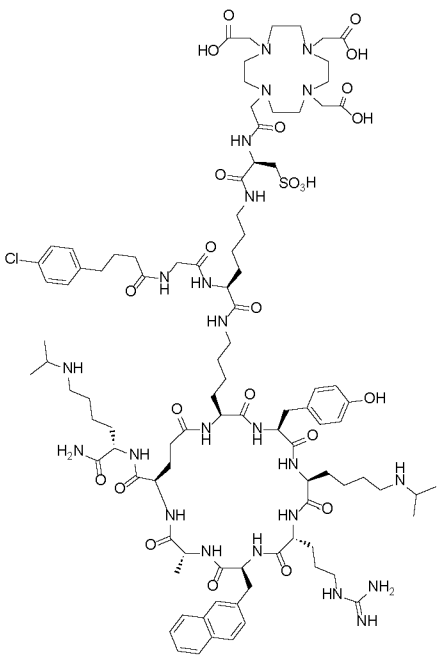

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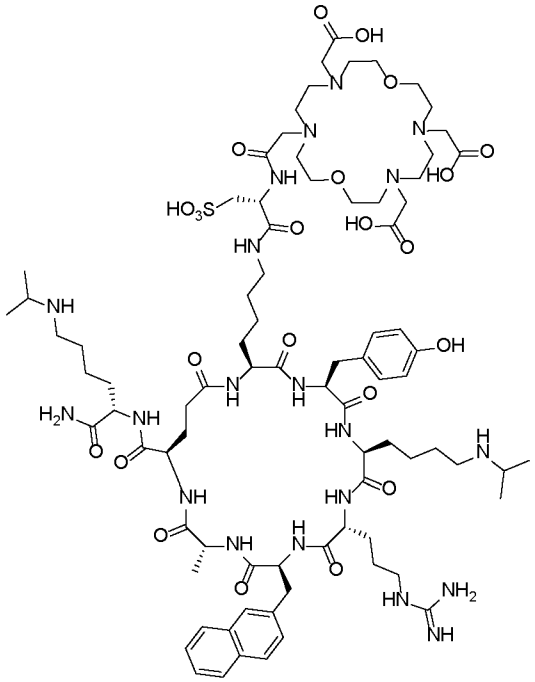


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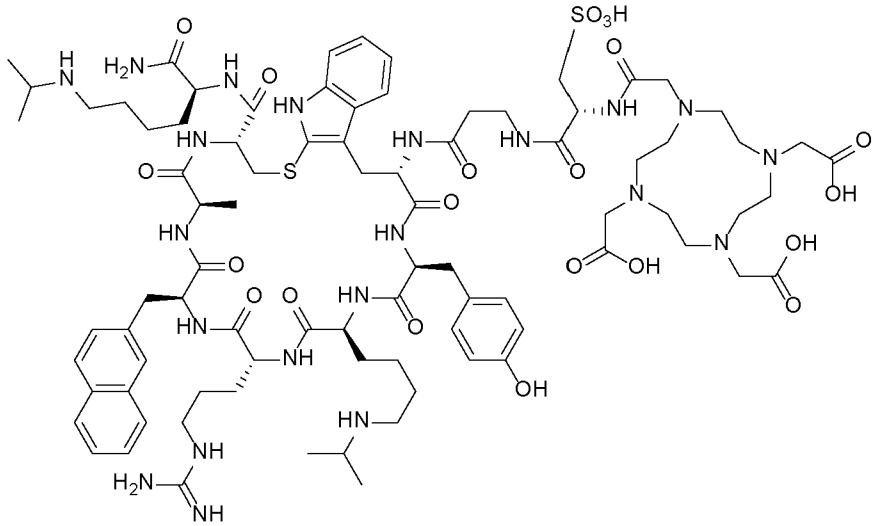
or a salt or solvate thereof. In some embodiments, the compound is complexed with a radioisotope.

[0573] In some embodiments of the compounds of Formula A, the compound is:

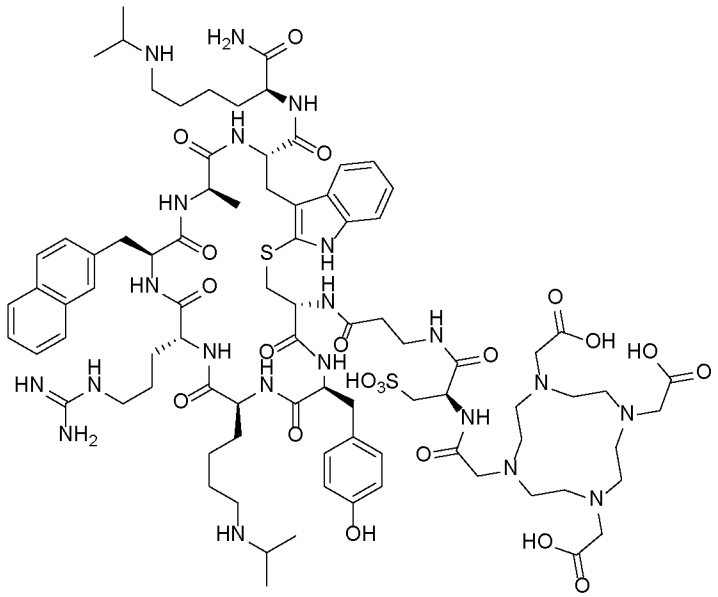


, or a salt or solvate thereof. In some embodiments, the compound is complexed with a radioisotope.

[0574] In some embodiments of the compounds of Formula B, the compound is:

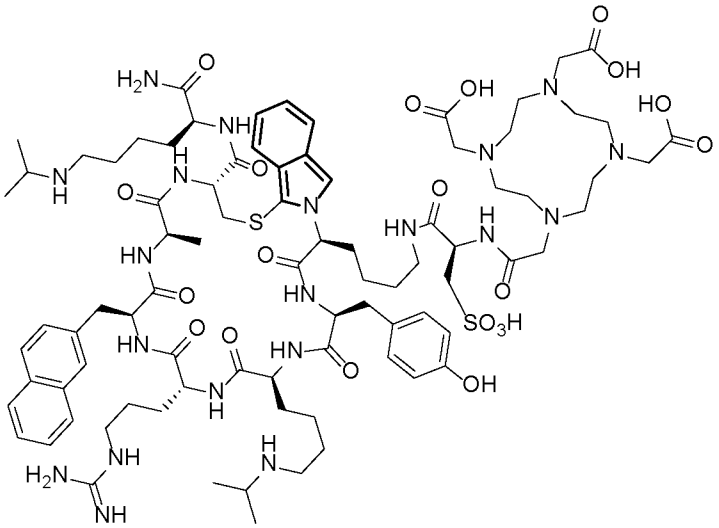


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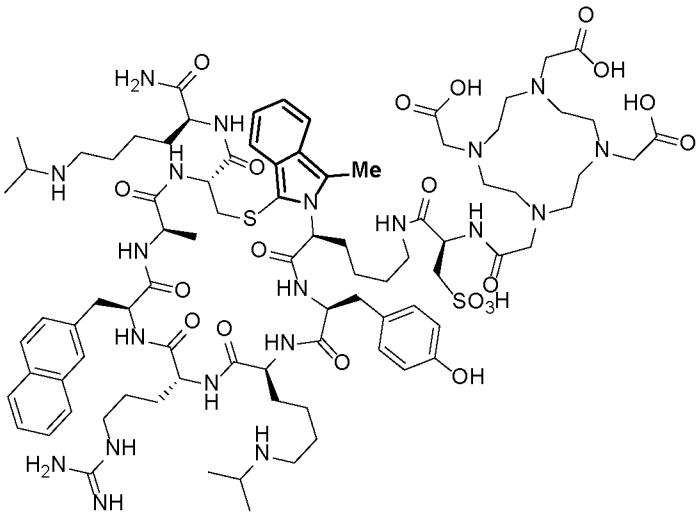


, or a salt or solvate thereof. In some embodiments, the compound is complexed with a radioisotope.

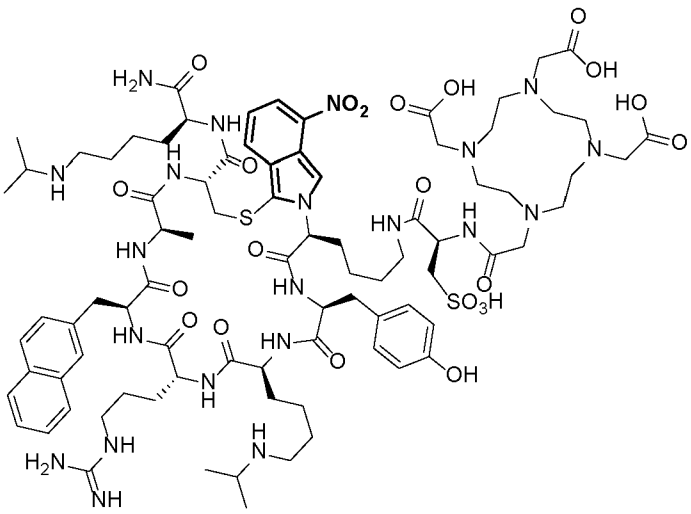
[0575] In some embodiments of the compounds of Formula C, the compound is:



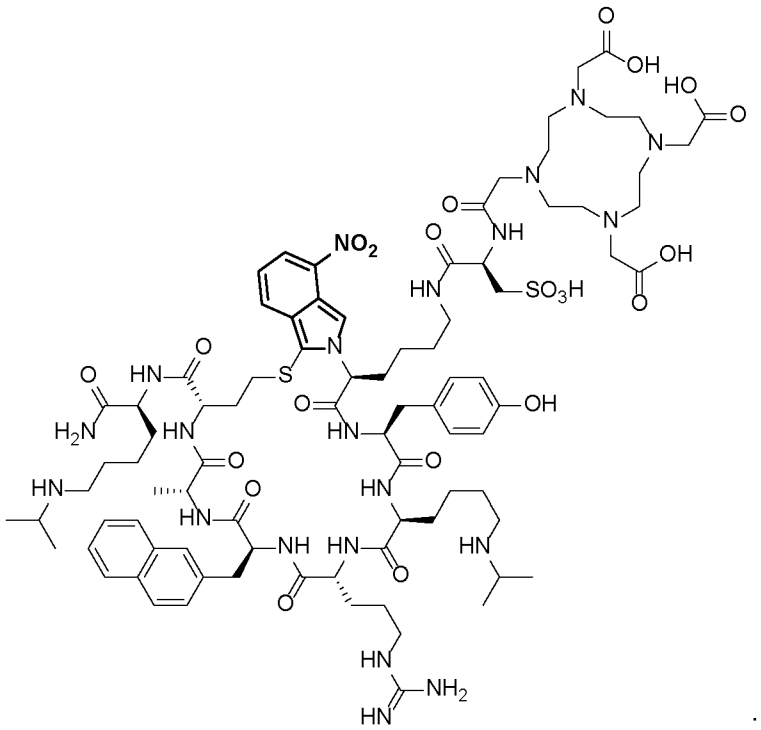
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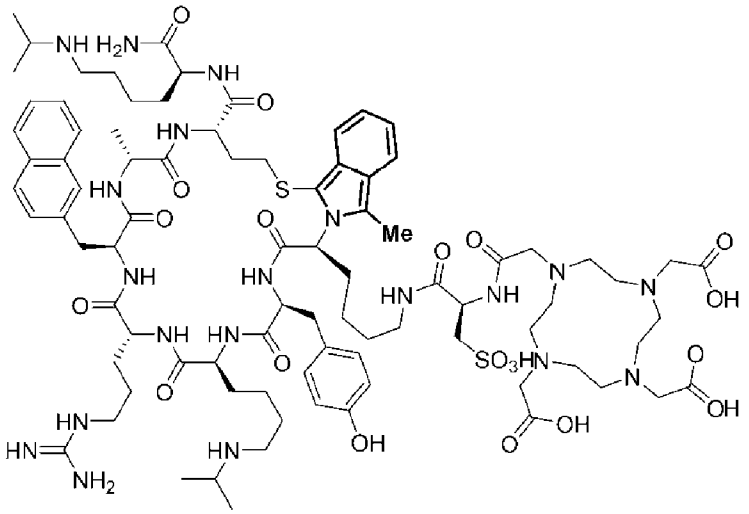
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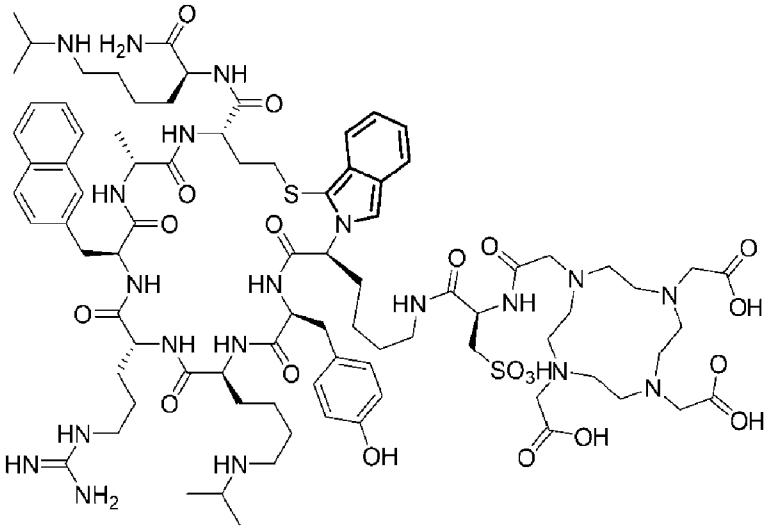
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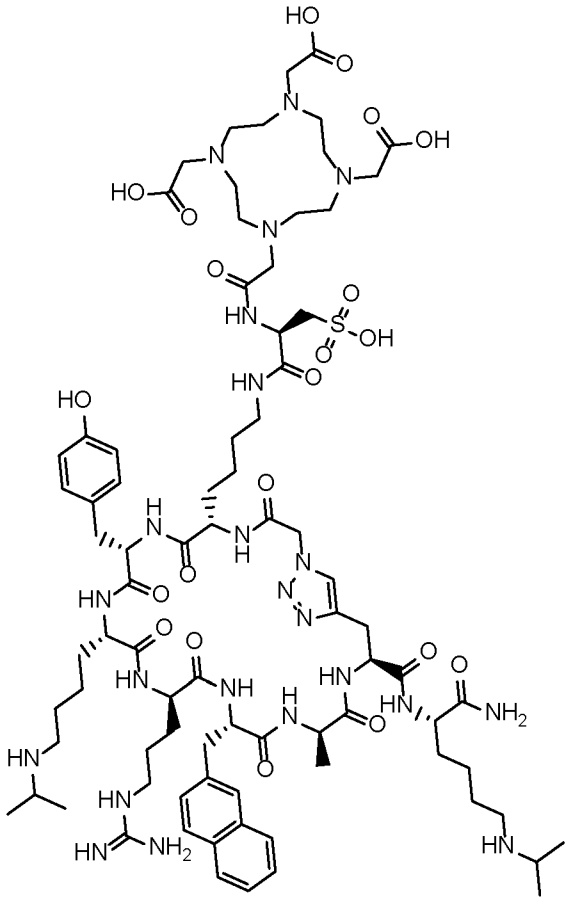
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; or



, or a salt or solvate thereof. In some embodiments, the compound is complexed with a radioisotope.

Methods of Use

[0576] The present disclosure also relates to any one of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4 as described herein, for use

in imaging a CXCR4-expressing tissue in a subject or for imaging an inflammatory condition or disease. In one embodiment, the compound comprises at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope, the compound is bound to a metal chelator complexed with an imaging radioisotope, or the compound is bound to a prosthetic group containing BF_3 comprising an imaging radioisotope. In one embodiment, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I, ^{152}Tb, ^{155}Tb, or ^{72}As. In one embodiment, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{131}I, ^{123}I, ^{124}I or ^{72}As.

[0577] The present disclosure also relates to a method of imaging a CXCR4-expressing tissue, comprising administering an effective amount of any one of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4 as described herein, to a subject in need of such imaging. In one embodiment, the compound comprises at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope, the compound is bound to a metal chelator complexed with an imaging radioisotope, or the compound is bound to a prosthetic group containing BF_3 comprising an imaging radioisotope. In one embodiment, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I, ^{152}Tb, ^{155}Tb, or ^{72}As. In one embodiment, the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{131}I, ^{123}I, ^{124}I or ^{72}As.

[0578] The present disclosure also relates to any one of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4 as described herein, for use in treating a disease or condition characterized by expression of CXCR4 in a subject. In one embodiment, the disease or condition is a CXCR4-expressing cancer. In one embodiment, the compound comprises at least one R^X comprises an imaging radioisotope or the compound is complexed with a therapeutic radioisotope, or the compound is bound to a metal chelator complexed with a therapeutic radioisotope. In one embodiment, the therapeutic radioisotope is ^{165}Er, ^{212}Bi, ^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu, ^{111}In, ^{213}Bi, ^{212}Pb, ^{47}Sc, ^{90}Y, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac, ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu or ^{67}Cu.

[0579] The present disclosure also relates to a method of treating a disease or condition characterized by expression of CXCR4, comprising administering an effective amount of any one of the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4 as described herein, to a subject in need thereof. In one embodiment, the disease or condition is a CXCR4-expressing cancer. In one embodiment, the compound comprises at least one R^X comprises an imaging radioisotope or the compound is complexed with a therapeutic radioisotope, or the compound is bound to a metal chelator complexed with a therapeutic radioisotope. In one embodiment, the therapeutic radioisotope is ^{165}Er, ^{212}Bi,

^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu, ^{111}In, ^{213}Bi, ^{212}Pb, ^{47}Sc, ^{90}Y, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac, ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu or ^{67}Cu.

[0580] In some embodiments, the compounds of Formula A, A-I, A-II, A-III, A-IV, B, or C, or Table 2 or derivatives thereof, or Table 4, inhibit SDF-1α binding to CXCR4 *in vitro* with an IC_{50} of 50 nM or lower. In some embodiments, the compounds inhibit SDF-1α binding to CXCR4 *in vitro* with an IC_{50} of 25 nM or lower. In some embodiments, the compounds inhibit SDF-1α binding to CXCR4 *in vitro* with an IC_{50} of 10 nM or lower.

[0581] The overexpression of CXCR4 has been observed in over 23 types of malignancies, including brain, breast, and prostate cancers. Moreover, leukemia, lymphoma and myeloma have significant CXCR4 expression. Retrospective studies have shown that CXCR4 expression is correlated with lowered survival for prostate and melanoma patients. Furthermore, CXCR4 expression is a prognostic factor of disease relapse for acute and chronic myeloid leukemia, acute myelogenous leukemia and multiple myeloma. The SDF-1/CXCR4 axis mediates cancer growth, potentiates metastasis, recruits stromal and immune cells to support malignant growth, and confers chemotherapeutic resistance. Radiolabeled CXCR4 probes could be used in the early diagnosis of solid and hematological malignancies that express CXCR4. Such imaging agents could be used to confirm the diagnostic of malignancy, or guide focal ablative treatment if the disease is localized. Such ligands could also be used to monitor response to therapy, by providing an independent assessment of the residual cellular content of a tumour known to overexpress CXCR4. [^{68}Ga]Ga-Pentixafor has been used by the Wester group for cancer imaging and to identify potential responders to endoradiotherapy.

[0582] Dysregulation of the SDF-1/CXCR4 axis also mediates a number of inflammatory conditions. In rheumatoid arthritis (RA), SDF-1/CXCR4 signaling is responsible for the pro-inflammatory migration of activated T-cells into the site of inflammation; specifically, the synovium of patients with RA showed that the presence of T-cells with increased expression of CXCR4. Given the burden of RA on the population with respect to morbidity and mortality, there is a significant amount of research into developing therapeutics to mediate the inflammatory response, especially with novel biologics being approved by the FDA in the past few years. Radiolabeled CXCR4 probes for positron emission tomography imaging would enable diagnosis and prognosis of the rheumatoid arthritis and also be used to monitor therapy of emerging disease-modifying antirheumatic drugs in clinical trials. CXCR4 expression has been detected with PET imaging using [^{68}Ga]Ga-Pentixafor in diseases with an inflammatory component, including infectious bone diseases, urinary tract infections as a complication after kidney transplantation, myocardial infarctions, and ischemic strokes. CXCR4 imaging may have a significant role in diagnosing and monitoring other inflammatory diseases in the future.

[0583] In the setting of cardiac pathology, inflammatory diseases of the cardiac vessel walls are mediated in part by the dysregulation of the SDF-1/CXCR4 axis. In the early stages of atherosclerosis, the SDF-1/CXCR4 axis recruits endothelial progenitor cells towards sites of peripheral vascular damage, thereby initiating plaque formation, though there is some evidence towards an atheroprotective effect. Atherosclerotic plaques are characterized by the presence of hypoxia, which has been shown to upregulate the expression of CXCR4 and influence cell trafficking. Finally, in a rabbit model of atherosclerosis, [^{68}Ga]Ga-Pentixafor enabled visualization of atherosclerotic plaques by PET. In the same study, atherosclerotic plaques were identified in patients with a history of atherosclerosis using [^{68}Ga]Ga-Pentixafor. As such, PET diagnostic agents targeting CXCR4 are potentially viable as an alternative method of diagnosing and obtaining prognostic information about atherosclerosis.

[0584] In some embodiments, the disease or condition characterized by expression of CXCR4 is leukemia, lymphoma and myeloma. In some embodiments, the disease or condition characterized by expression of CXCR4 is a hematological malignany. In some embodiments, the disease or condition characterized by expression of CXCR4 is an inflammatory disease. In some embodiments, inflammatory disease is atherosclerosis.

[0585] In some embodiments, the disease or condition characterized by expression of CXCR4 is a cardiovaacular disease.

[0586] In some embodiments, the disease or condition characterized by expression of CXCR4 is a disease or condition characterized by an overexpression of CXCR4 or an abnormal expression of CXCR4.

[0587] In some embodment, the CXCR4-expressing cancer is a hematologic malignancy. In some embodment, the CXCR4-expressing cancer is leukemia, lymphoma and myeloma.

[0588] In certain embodiments, the compound of Formula A, A-I, A-II, A-III, A-IV, B, or C is conjugated with a radioisotope for positron emission tomography (PET) or single photon emission computed tomography (SPECT) imaging of a CXCR4-expressing tissue or for imaging an inflammatory condition or disease (e.g. rheumatoid arthritis or cardiovascular disease), wherein the compound is conjugated with a radioisotope that is a positron emitter or a gamma emitter. Without limitation, the positron or gamma emitting radioisotope may be ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{110m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I or ^{72}As.

[0589] When the radioisotope (e.g. X) is a diagnostic radioisotope, there is disclosed use of certain embodiments of the compound for preparation of a radiolabelled tracer for imaging. There is also disclosed a method of imaging CXCR4-expressing tissues or an inflammatory condition or disease in a subject, in which the method comprises: administering to the subject a composition comprising certain embodiments of the compound and a pharmaceutically acceptable excipient; and imaging the subject, e.g. using positron emission tomography (PET). When the tissue is a diseased tissue (e.g. a CXCR4-expressing cancer), CXCR4-

targeted treatment may then be selected for treating the subject. There is therefore disclosed the use of certain compounds of the invention in imaging a CXCR4-expressing cancer in a subject, wherein R^X comprises or is complexed with a diagnostic or imaging radioisotope. In some embodiments, the subject is human.

[0590] Given the broad expression of CXCR4 in cancers, there has been a significant push to develop CXCR4-targeting therapeutics. While CXCR4 inhibitors have demonstrated efficacy in tumor models in mice, in both treating tumors and preventing metastasis, very few pharmaceutical agents have demonstrated efficacy in clinical trials. Plerixafor, also known as AMD3100, developed originally for HIV treatment, is the lone CXCR4 antagonist to receive FDA approval to date. AMD3100 is given to lymphoma and multiple myeloma patients to mobilize hematopoietic stem cells into peripheral blood for collection and autologous transplantation, and not as a method of direct treatment. There is an unmet clinical need for treating CXCR4-expressing cancers, many of which are resistant to the standard of care available today.

[0591] Cancers that are CXCR4 positive could be susceptible to endoradiotherapy. In this application, a peptide targeting CXCR4 is radiolabeled with a radioisotope, usually a β- or α-particle emitter, to deliver a high local dose of radiation to lesions. These radioactive emissions usually inflict DNA damage, thereby inducing cellular death. This method of therapy has been exploited in oncology, with the somatostatin receptor (for neuroendocrine tumors) and prostate-specific membrane antigen (for metastatic castration-resistant prostate cancer) being two examples. Unlike external beam radiation therapy, this systemic treatment can be effective even in the metastatic setting. Therapeutic radioisotopes include but are not restricted to ^{177}Lu, ^{90}Y, ^{225}Ac and ^{64}Cu.

[0592] With respect to cardiac pathologies, a small retrospective study with endoradiotherapy by [^{90}Y]Y- or [^{177}Lu]Lu-Pentixather demonstrated regression of CXCR4 expression and activity in patients with previously identified atherosclerotic plaques. Therefore, radionuclide therapy may present a novel route of therapy for inflammatory diseases such as atherosclerosis.

[0593] In certain embodiments the compound of Formula A, A-I, A-II, A-III, A-IV, B, or C is conjugated with a radioisotope that is used for therapy (e.g. cancer therapy). This includes radioisotopes such as ^{165}Er, ^{212}Bi, ^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu (β-emitter, $t_{2/1}$ = 6.65 d), ^{111}In, ^{213}Bi, ^{212}Pb, ^{47}Sc, ^{90}Y (β-emitter, $t_{2/1}$ = 2.66 d), ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac (α-emitter, $t_{2/1}$ = 9.95 d), ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu or ^{67}Cu.

[0594] When the radioisotope (e.g. X) is a therapeutic radioisotope, there is disclosed use of certain embodiments of the compound (or a pharmaceutical composition thereof) for the treatment of a disease or condition characterized by expression of CXCR4 in a subject. Accordingly, there is provided use of the compound in preparation of a medicament for treating a disease or condition characterized by expression of CXCR4 in a subject. There is also

provided a method of treating a disease or condition characterized by expression of CXCR4 in a subject, in which the method comprises: administering to the subject a composition comprising the compound of Formula A, A-I, A-II, A-III, A-IV, B, or C, or a salt or solvate thereof and a pharmaceutically acceptable excipient. For example, but without limitation, the disease may be a CXCR4-expressing cancer (e.g. non-Hodgkin lymphoma, lymphoma, multiple myeloma, leukemia, adrenocortical cancer, lung cancer, breast cancer, renal cell cancer, colorectal cancer). There is therefore disclosed the use of certain compounds of the invention for treating a CXCR4-expressing cancer in a subject, wherein R^X comprises or is complexed with a therapeutic radioisotope. In some embodiments, the subject is human.

Methods of Manufacturing

[0595] The compounds presented herein incorporate peptides, which may be synthesized by any of a variety of methods established in the art. This includes but is not limited to liquid-phase as well as solid-phase peptide synthesis using methods employing 9-fluorenylmethoxycarbonyl (Fmoc) and/or t-butyloxycarbonyl (Boc) chemistries, and/or other synthetic approaches.

[0596] Solid-phase peptide synthesis methods and technology are well-established in the art. For example, peptides may be synthesized by sequential incorporation of the amino acid residues of interest one at a time. In such methods, peptide synthesis is typically initiated by attaching the C-terminal amino acid of the peptide of interest to a suitable resin. Prior to this, reactive side chain and alpha amino groups of the amino acids are protected from reaction by suitable protecting groups, allowing only the alpha carboxyl group to react with a functional group such as an amine group, a hydroxyl group, or an alkyl halide group on the solid support. Following coupling of the C-terminal amino acid to the support, the protecting group on the side chain and/or the alpha amino group of the amino acid is selectively removed, allowing the coupling of the next amino acid of interest. This process is repeated until the desired peptide is fully synthesized, at which point the peptide can be deprotected and cleaved from the support, and purified. A non-limiting example of an instrument for solid-phase peptide synthesis is the Aapptec Endeavor 90 peptide synthesizer.

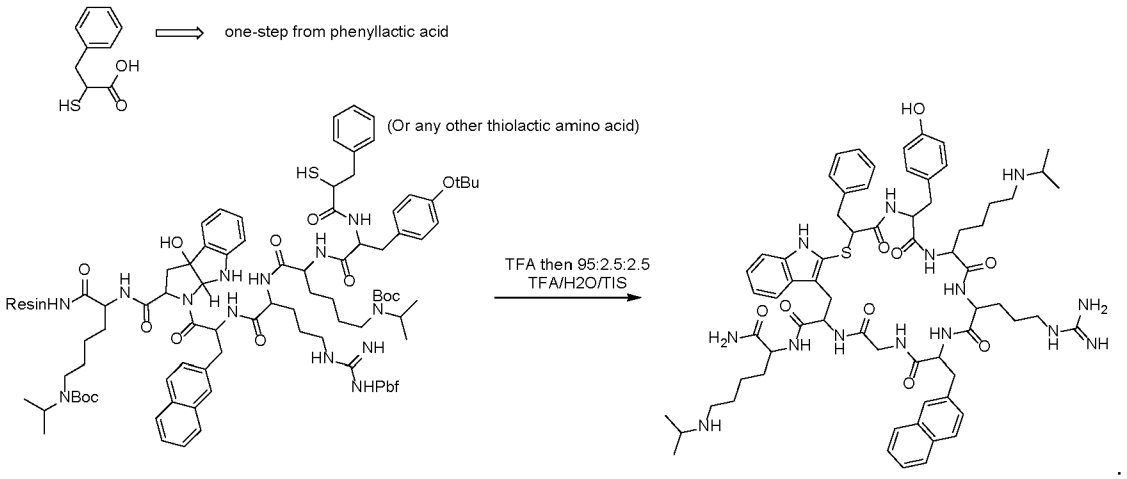
[0597] To allow coupling of additional amino acids, Fmoc protecting groups may be removed from the amino acid on the solid support, e.g. under mild basic conditions, such as piperidine (20-50% v/v) in DMF. The amino acid to be added must also have been activated for coupling (e.g. at the alpha carboxylate). Non-limiting examples of activating reagents include without limitation 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), benzotriazole-1-yl-oxy-tris(dimethylamino)phosphoniumhexafluorophosphate (BOP), benzotriazole-1-yl-

oxy-tris(pyrrolidino)phosphoniumhexafluorophosphate (PyBOP). Racemization is minimized by using triazoles, such as 1-hydroxy-benzotriazole (HOBt) and 1-hydroxy-7-aza-benzotriazole (HOAt). Coupling may be performed in the presence of a suitable base, such as N,N-diisopropylethylamine (DIPEA/DIEA) and the like. For long peptides or if desired, peptide synthesis and ligation may be used.

[0598] Apart from forming typical peptide bonds to elongate a peptide, peptides may be elongated in a branched fashion by attaching to side chain functional groups (e.g. carboxylic acid groups or amino groups), either: side chain to side chain; or side chain to backbone amino or carboxylate. Coupling to amino acid side chains may be performed by any known method, and may be performed on-resin or off-resin. Non-limiting examples include: forming an amide between an amino acid side chain containing a carboxyl group (e.g. Asp, D-Asp, Glu, D-Glu, Aad, and the like) and an amino acid side chain containing an amino group (e.g. Lys, D-Lys, Orn, D-Orn, Dab, D-Dab, Dap, D-Dap, and the like) or the peptide N-terminus; forming an amide between an amino acid side chain containing an amino group (e.g. Lys, D-Lys, Orn, D-Orn, Dab, D-Dab, Dap, D-Dap, and the like) and either an amino acid side chain containing a carboxyl group (e.g. Asp, D-Asp, Glu, D-Glu, and the like) or the peptide C-terminus; and forming a 1, 2, 3-triazole via click chemistry between an amino acid side chain containing an azide group (e.g. Lys(N_3), D-Lys(N_3), and the like) and an alkyne group (e.g. Pra, D-Pra, and the like). The protecting groups on the appropriate functional groups must be selectively removed before amide bond formation, whereas the reaction between an alkyne and an azido groups via the click reaction to form an 1,2,3-triazole does not require selective deprotection. Non-limiting examples of selectively removable protecting groups include 2-phenylisopropyl esters (O-2-PhiPr) (e.g. on Asp/Glu) as well as 4-methyltrityl (Mtt), allyloxycarbonyl (alloc), 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene))ethyl (Dde), and 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-methylbutyl (ivDde) (e.g. on Lys/Orn/Dab/Dap). O-2-PhiPr and Mtt protecting groups can be selectively deprotected under mild acidic conditions, such as 2.5% trifluoroacetic acid (TFA) in DCM. Alloc protecting groups can be selectively deprotected using tetrakis(triphenylphosphine)palladium(0) and phenylsilane in DCM. Dde and ivDde protecting groups can be selectively deprotected using 2-5% of hydrazine in DMF. Deprotected side chains of Asp/Glu (L- or D-forms) and Lys/Orn/Dab/Dap (L- or D-forms) can then be coupled, e.g. by using the coupling reaction conditions described above.

[0599] Formula A, A-I, A-II, A-III, and A-IV compounds may be cyclized by linking the peptide N-terminus to a side chain carboxylate (at residue 7 in the peptide) using the technologies discussed above (exemplary reaction conditions are described in the Examples). Formula B compounds may be cyclized using an intra-annular tryptathionine stapling reaction or an isoindole stapling reaction, called FIICk[21], to link the side chains of residues 1 and 7 in the peptide (exemplary reaction conditions are described in the Examples); the resulting

isoindoles have intrinsic fluorescent properties imaging. Formula C compounds may be similarly cyclized using a thiolactic amino acid at residue 1 in the peptide, e.g. as shown in the following scheme:



[0600] Peptide backbone amides may be N-methylated (i.e. alpha amino methylated). This may be achieved by directly using Fmoc-N-methylated amino acids during peptide synthesis. Alternatively, N-methylation under Mitsunobu conditions may be performed. First, a free primary amine group is protected using a solution of 4-nitrobenzenesulfonyl chloride (Ns-Cl) and 2,4,6-trimethylpyridine (collidine) in NMP. N-methylation may then be achieved in the presence of triphenylphosphine, diisopropyl azodicarboxylate (DIAD) and methanol. Subsequently, N-deprotection may be performed using mercaptoethanol and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in NMP. For coupling protected amino acids to N-methylated alpha amino groups, HATU, HOAt and DIEA may be used.

[0601] The formation of the thioether (-S-) linkages (e.g. for L^1) can be achieved either on solid phase or in solution phase. For example, the formation of thioether (-S-) linkage can be achieved by coupling between a thiol-containing compound (such as the thiol group on cysteine side chain) and an alkyl halide (such as 3-(Fmoc-amino) propyl bromide and the like) in an appropriate solvent (such as N,N-dimethylformamide and the like) in the presence of base (such as N,N-diisopropylethylamine and the like). If the reactions are carried out in solution phase, the reactants used are preferably in equivalent molar ratio (1 to 1), and the desired products can be purified by flash column chromatography or high performance liquid chromatography (HPLC). If the reactions are carried out on solid phase, meaning one reactant has been attached to a solid phase, then the other reactant is normally used in excess amount (≥ 3 equivalents of the reactant attached to the solid phase). After the reactions, the excess unreacted reactant and reagents can be removed by sequentially washing the solid phase (resin) using a combination of solvents, such as N,N-dimethylformamide, methanol and dichloromethane, for example.

[0602] The formation of the linkage (e.g. for L^1) between a thiol group and a maleimide group can be performed using the conditions described above for the formation of the thioether (-S-) linkage simply by replacing the alkyl halide with a maleimide-containing compounds. Similarly, this reaction can be conducted in solid phase or solution phase. If the reactions are carried out in solution phase, the reactants used are preferably in equivalent molar ratio (1 to 1), and the desired products can be purified by flash column chromatography or high performance liquid chromatography (HPLC). If the reactions are carried out on solid phase, meaning one reactant has been attached to a solid phase, then the other reactant is normally used in excess amount (≥ 3 equivalents of the reactant attached to the solid phase). After the reactions, the excess unreacted reactant and reagents can be removed by sequentially washing the solid phase (resin) using a combination of solvents, such as N,N-dimethylformamide, methanol and dichloromethane, for example.

[0603] Non-peptide moieties (e.g. radiolabeling groups, albumin-binding groups and/or linkers) may be coupled to the peptide N-terminus while the peptide is attached to the solid support. This is facile when the non-peptide moiety comprises an activated carboxylate (and protected groups if necessary) so that coupling can be performed on resin. For example, but without limitation, a bifunctional chelator, such as 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) tris(tert-butyl ester) may be activated in the presence of N-hydroxysuccinimide (NHS) and N,N'-dicyclohexylcarbodiimide (DCC) for coupling to a peptide. Alternatively, a non-peptide moiety may be incorporated into the compound via a copper-catalyzed click reaction under either liquid or solid phase conditions. Copper-catalyzed click reactions are well established in the art. For example, 2-azidoacetic acid is first activated by NHS and DCC and coupled to a peptide. Then, an alkyne-containing non-peptide moiety may be clicked to the azide-containing peptide in the presence of Cu^{2+} and sodium ascorbate in water and organic solvent, such as acetonitrile (ACN) and DMF and the like. Non-peptide moieties may also be added in solution phase, which is routinely performed.

[0604] The synthesis of chelators is well-known and many chelators are commercially available (e.g. from Sigma-Aldrich™/Milipore Sigma™ and others). Protocols for conjugation of radiometals to the chelators are also well known (e.g. see Example 1, below). The synthesis of the silicon-fluorine-acceptor moieties can be achieved following previously reported procedures (e.g. Bernard-Gauthier et al. *Biomed Res Int.* 2014 2014:454503; Kostikov et al. *Nature Protocols* 2012 7:1956–1963; Kostikov et al. *Bioconjug Chem.* 2012 18:23:106-114; each of which is incorporated by reference in its entirety). The synthesis or acquisition of radioisotope-substituted aryl groups is likewise facile.

[0605] The synthesis of the $R^{13}R^{14}BF_3$ component on the compounds can be achieved following previously reported procedures (e.g.: Liu *et al. Angew Chem Int Ed* 2014 53:11876-11880; Liu *et al. J Nucl Med* 2015 55:1499-1505; Liu *et al. Nat Protoc* 2015 10:1423-1432;

Kuo *et al., J Nucl Med* 2019 60:1160-1166; each of which is incorporated by reference in its entirety). Generally, the BF_3-containing motif can be coupled to the linker via click chemistry by forming a 1,2,3-triazole ring between a BF_3-containg azido (or alkynyl) group and an alkynyl (or azido) group on the linker, or by forming an amide linkage between a BF_3-containg carboxylate and an amino group on the linker. To make the BF_3-containing azide, alkyne or carboxylate, a boronic acid ester-containing azide, alkyne or carboxylate is first prepared following by the conversion of the boronic acid ester to BF_3 in a mixture of HCl, DMF and KHF_2. For alkyl BF_3, the boronic acid ester-containing azide, alkyne or carboxylate can be prepared by coupling boronic acid ester-containing alkyl halide (such as iodomethylboronic acid pinacol ester) with an amine-containing azide, alkyne or carboxylate (such as N,N-dimethylpropargylamine). For aryl BF_3, the boronic acid ester can be prepared via Suzuki coupling using aryl halide (iodine or bromide) and bis(pinacolato)diboron.

[0606] ^{18}F-Fluorination of the BF_3-containing compounds via ^{18}F-^{19}F isotope exchange reaction can be achieved following previously published procedures (Liu *et al. Nat Protoc* 2015 10:1423-1432, incorporated by reference in its entirety). Generally, ~100 nmol of the BF_3-containing compound is dissolved in a mixture of 15 µl of pyridazine-HCl buffer (pH = 2.0–2.5, 1 M), 15 µl of DMF and 1 µl of a 7.5 mM KHF_2 aqueous solution. ^{18}F-Fluoride solution (in saline, 60 µl) is added to the reaction mixture, and the resulting solution is heated at 80 °C for 20 min. At the end of the reaction, the desired product can be purified by solid phase extraction or by reversed high performance liquid chromatography (HPLC) using a mixture of water and acetonitrile as the mobile phase.

[0607] When the peptide has been fully synthesized on the solid support, the desired peptide may be cleaved from the solid support using suitable reagents, such as TFA, tri-isopropylsilane (TIS) and water. Side chain protecting groups, such as Boc, pentamethyldihydrobenzofuran-5-sulfonyl (Pbf), trityl (Trt) and tert-butyl (tBu) are simultaneously removed (i.e. deprotection). The crude peptide may be precipitated and collected from the solution by adding cold ether followed by centrifugation. Purification and characterization of the peptides may be performed by standard separation techniques, such as high performance liquid chromatography (HPLC) based on the size, charge and polarity of the peptides. The identity of the purified peptides may be confirmed by mass spectrometry or other similar approaches.

[0608] The present invention will be further illustrated in the following examples for the synthesis and evaluation of specific compounds.

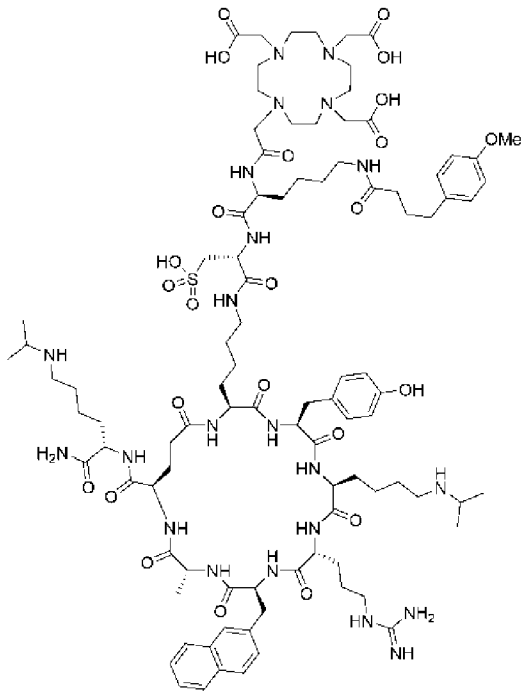
EXAMPLES

Chemical Synthesis

[0609] Experimental:

[0610] Reagents and solvents were purchased from commercial sources and used without further purification, unless otherwise stated. Peptides were synthesized on a Liberty Blue automated microwave peptide synthesis (CEM Corporations) or on a PurePep Chorus GT (Gyros Protein Technologies). High performance liquid chromatography (HPLC) was performed on (1) an Agilent 1260 infinity system equipped with a model 1200 quaternary pump, a model 1200 UV absorbance detector and a Bioscan NaI scintillation detector, (2) an Agilent 1100 HPLC system or (3) an Agilent 1260 Infinity II Preparative System equipped with a model 1260 Infinity II preparative binary pump, a model 1260 Infinity variable wavelength detector (set at 220 nm), and a 1290 Infinity II preparative open-bed fraction collector. The HPLC column used for synthesis was a semi-preparative column (Agilent Eclipse XDB-C18, 5µm, 9.4x250mm) or a preparative column (Gemini, NX-C18, 5 µm, 110 Å, 50x30 mm) purchased from Phenomenex. Mass analyses were performed using an AB SCIEX 4000 QTRAP mass spectrometer system with an ESI ion source or a Waters 2695 Separation module and a Waters-Micromass ZQ mass spectrometer system.

[0611] Synthesis of BL34L6

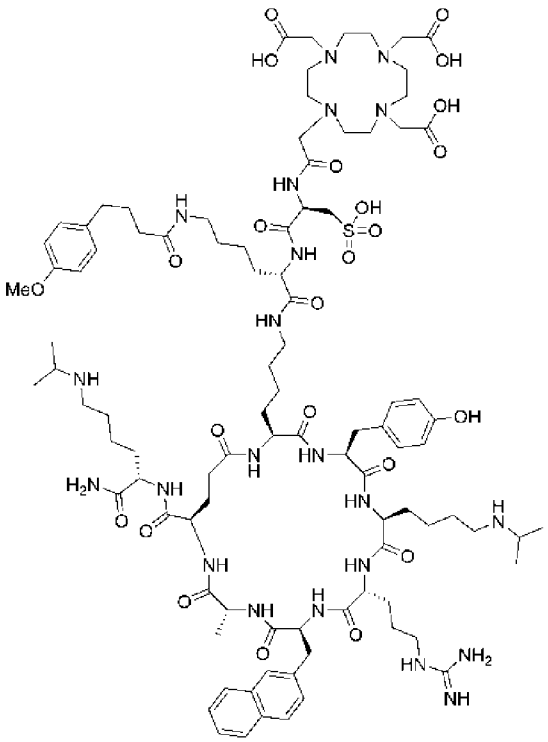


BL34L6

[0612] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-

Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll (allyloxy) group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-cysteic acid and Fmoc-Lys(ivDde)-OH were coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/HOAt/DIPEA (4/4/8 eq.), followed by ivDde deprotection, and 4-(4-methoxyphenyl)butanoic acid coupling with HATU/HOAt/DIPEA (4/4/8 eq.). The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/MeCN mixture. The crude peptide was purified with semi-prep HPLC column using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 4.5 mL/min. (31% B over 20 min, t_R = 7.189 min). The sample was lyophilized to a white solid. Calc mass ($M+H^+$): 2026.08 m/z; found ($M + 3H^+$)/3: 676.21 m/z.

[0613] Synthesis of BL34L7

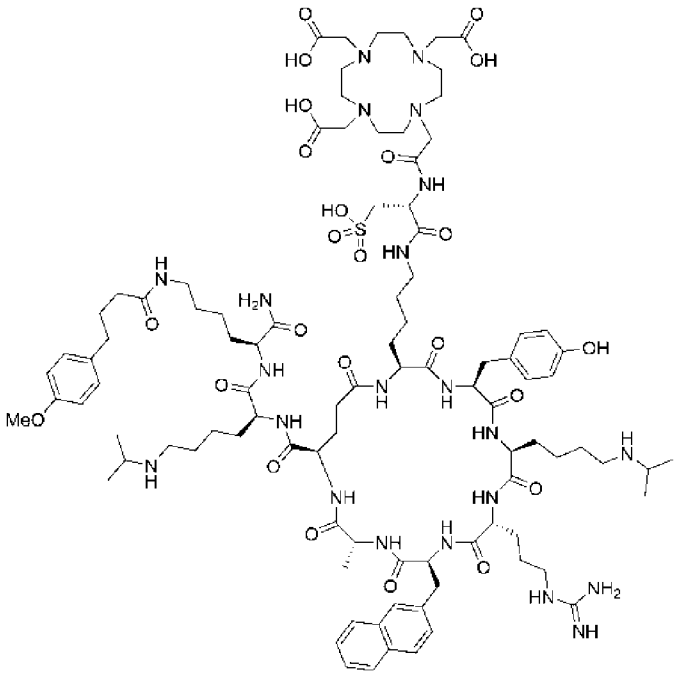


BL34L7

[0614] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-

Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-Lys(ivDde)-OH and Fmoc-cysteic acid were coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/HOAt/DIPEA (4/4/8 eq.), followed by ivDde deprotection, and 4-(4-methoxyphenyl)butanoic acid coupling with HATU/HOAt/DIPEA (4/4/8 eq.). The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/ACN mixture. The crude peptide was purified with a semi-prep HPLC column using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 4.5 mL/min. (31% B over 20 min, t_R = 6.796 min). The sample was lyophilized to a white solid. Calc mass ($M+H^+$): 2026.08 m/z; found $(M + 3H)^{3+}/3$: 676.21 m/z.

[0615] Synthesis of BL34L8

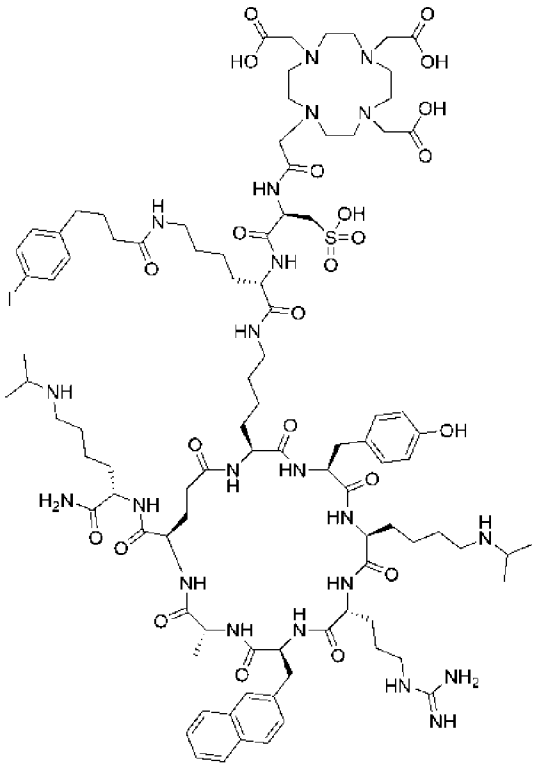


BL34L8

[0616] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x3). Then, Fmoc-Lys(Mtt)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 75°C (12 min) using HATU/HOAt/DIPEA (5/5/10 eq.) twice. The resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1

min), and then washed with DMF (3 mL x3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-cysteic acid was coupled as described above. Following Fmoc-deprotection, DOTA (4 eq.) was coupled using HATU/HOAt/DIPEA (4/4/8 eq.). After that, the Mtt protecting group was removed with 2% TFA in DCM (4 mL, RT, 2 min, x8), washed with DCM (3 mL x 5) and DMF (4 mL x 5). The resin was neutralized with 10% DIPEA in DMF (5 mL, 5 min, twice) before coupling of 4-(4-methoxyphenyl)butanoic acid. The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/MeCN mixture. The crude peptide was purified with semi-prep HPLC column using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 4.5 mL/min. (31% B over 20 min, t_R = 5.827 min). Calc mass $(M+H^+)$: 2026.08 m/z; found $(M + 3H)^{3+}/3$: 676.41 m/z.

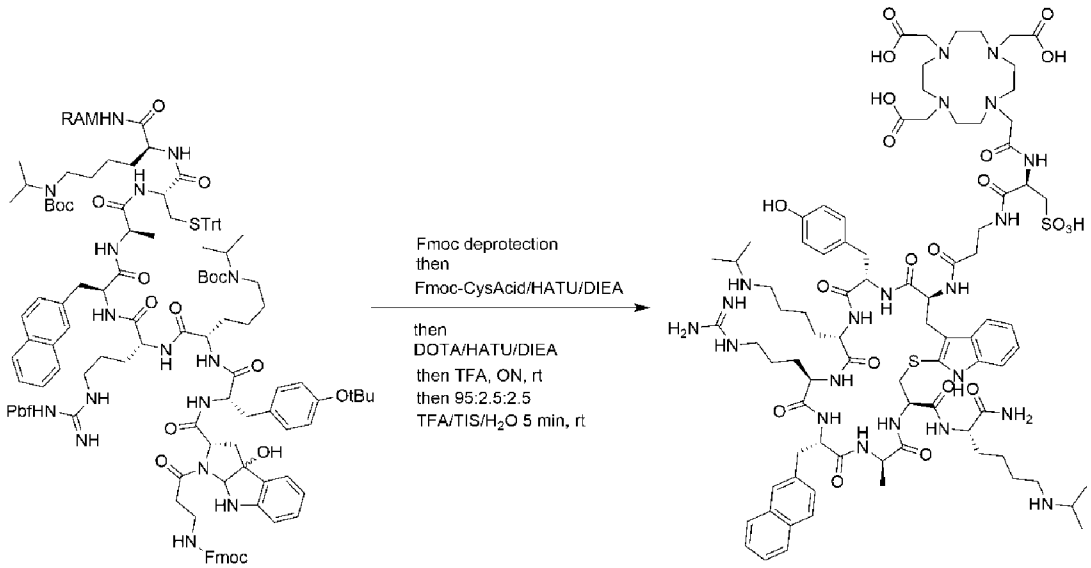
[0617] Synthesis of BL34L11



BL34L11

[0618] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x 3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-Lys(ivDde)-OH and Fmoc-cysteic acid were coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/HOAt/DIPEA (4/4/8 eq.), followed by ivDde deprotection, and 4-(4-iodophenyl)butanoic acid coupling with HATU/HOAt/DIPEA (4/4/8 eq.). The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/MeCN mixture. The crude peptide was purified with prep HPLC using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 30 mL/min (31% B over 15 min, t_R = 8.617 min). The sample was lyophilized to a white solid. Calc mass $(M+H^+)$: 2121.96 m/z; found $(M + 2H)^{2+}/2$: 1061.98 m/z.

[0619] Synthesis of Compound A



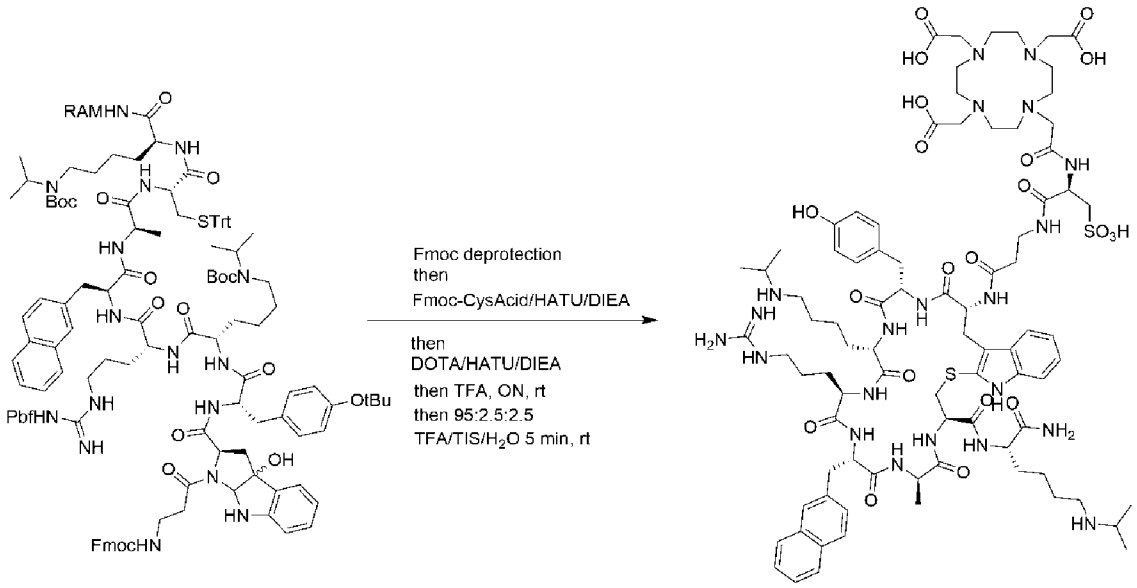
MT16-145-L-Hpi **Compound A**

[0620] Synthesis of MT16-145-L-Hpi: MBHA Rink Amide (0.04 mmol) resin was solvated in 3 mL of DMF and mixed by bubbling N_2 for 20 min and then drained. Resin was resuspended in 3 mL 20% Piperidine-DMF and mixed by bubbling N_2 for 1 min at 50°C, solution was drained,

and the process was repeated with a fresh 3 mL portion of DMF. Resin was washed three times with 3 mL portions of DMF (mixed by bubbling with N_2 and then drained.) Resin was resuspended in 3 mL DMF containing Fmoc-Xaa-OH (100 mM), HCTU (100 mM), N-methyl-morpholine (200 mM) with at least 7.5 equivalents of amino acid and coupling agent to initial resin loading. Resin suspended in coupling solution was mixed by bubbling with N_2 for 5 min at 50°C. Exceptions were as follows: Fmoc-aza-Xaa-OH dipeptides were mixed by bubbling with N_2 at 50°C for 50 min. Fmoc-Hpi-OH was mixed by bubbling with N_2 at RT for 1 h. Resin was washed 3 mL portions of DMF (x3) (mixed by N_2 bubbling and then drained.) After the last coupling, resin was then washed with 3 mL portions of DCM (x4) (mixed by N_2 bubbling and then drained.) The resin was then dried by flushing with N_2 for 20 min. Resin was suspended in 5 mL DMF on synthesizer manually, mixed with N_2 bubbling for 20 min, Fmoc deprotected on synthesizer, then washed with DMF (x3). A solution of 74.1 mg Fmoc-β-Ala-OH, 102.2 mg COMU, 0.12 mL DIEA in 1 mL DMF was added to reaction vessel, bubbled for ~1-1.5 h. Fresh coupling solution was prepared for each hour. The process was repeated three times resulting in total reaction time of 5.5 h. After last round of coupling, resin was washed with DCM (x4) and dried for 20 min on peptide synthesizer. The resin bound linear peptide was suspended in 5mL DMF on the synthesizer manually and mixed with N_2 bubbling for 20 min. Fmoc deprotected by treatment with 20% Piperidine-DMF (3 mL), mixed by N_2 bubbling. Resin was washed with DMF (x3). Incubated with 1:2:2 Ac_2O/EtOAc/Collidine (5 mL) for 30 min on synthesizer, then washed with DMF (x3), then washed with DCM (x4), then dried for 20 min. The dry resin was stirred in a round-bottom flask with 2 mL TFA overnight. In the morning, 50 µL TIS and 50 µL H_2O were added until the bright yellow colour disappeared. The TFA is filtered into a 15 mL falcon tube, triturated with Et_2O (x3), pellet allowed to dry under air and dissolved in H_2O/MeCN 0.1% FA and purified by HPLC on C18 with gradient elution using 0.1% FA H_2O/MeCN on 50x21mm column. Pure fraction collected, frozen and lyophilized. The pure peptide was re-injected using solvents A: H_2O/0.1% FA and B: MeCN/0.1% FA with an Agilent Eclipse XDDC18 C18 column (9.4x250 mm) eluted with first 95% H_2O to 65% H_2O with 0.1% FA from 0-32 min, then 65-0% H_2O with 0.1% FA for 32-35 min at a flow rate of 2 mL/min. (t_R = 23.362 min). LRMS-ESI (m/z): $C_{68}H_{98}N_{16}O_{11}S$ $(M+2H)^{2+}/2$ calc 673.4 m/z obs. 673.7 m/z.

[0621] Synthesis of Compound A: From the synthesis of MT16-145-L-Hpi, after the appendage of Fmoc-β-Ala-OH, Fmoc is deprotected by treatment with 20% Piperidine-DMF (3 mL), mixed by N_2 bubbling. Resin is washed with DMF (x3). Fmoc-cysteic acid is coupled and then DOTA at RT using HATU and DIEA in DMF using 4/4/8 equivalents. The dry resin is stirred in a round-bottom flask with 2 mL TFA overnight. In the morning, 50 µL TIS and 50 µL H_2O are added until the bright yellow colour disappeared. The TFA is filtered into a 15 mL falcon tube, triturated with Et_2O (x3), and the pellet is allowed to dry under air.

[0622] Synthesis of Compound B



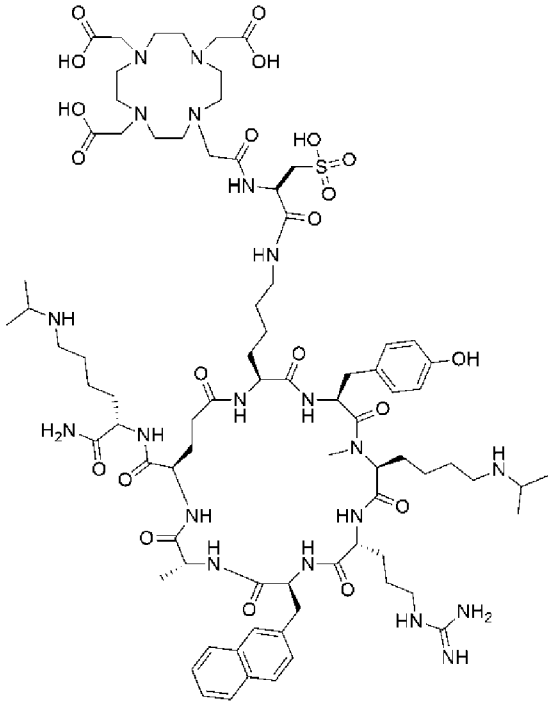
MT16-133-D-Hpi **Compound B**

[0623] Synthesis of MT16-145-D-Hpi: From the synthesis of MT16-145-L-Hpi, instead of Fmoc-L-Hpi, Fmoc-D-Hpi-OH was mixed by N_2 bubbling at RT for 1 hour. Resin was washed with 3 mL portions of DMF (x3) (mixed by N_2 bubbling and then drained.) After the last coupling, resin was then washed with 3 mL portions of DCM (x4) (mixed by N_2 bubbling and then drained.) The resin was dried by flushing with N_2 for 20 min. Resin was suspended in 5 mL DMF on synthesizer manually, mixed with N_2 bubbling for 20 min. Fmoc deprotected on synthesizer, then washed with DMF (x3). 74.1mg Fmoc-β-Ala-OH, 102.2mg COMU 0.12mL DIEA in 1 mL DMF added to reaction vessel, bubbled for ~1-1.5h. Fresh coupling solution made for each hour. Repeated x3 resulting in total reaction time of 5.5h. After last round of coupling, resin was washed with DCM (x4) and dried for 20 min on the peptide synthesizer. The resin bound linear peptide was suspended in 5mL DMF on the synthesizer manually and mixed with N_2 bubbling for 20 min. Fmoc deprotected by treatment with 20% Piperidine-DMF (3 mL), mixed by N_2 bubbling. Resin was washed with DMF (x3). Incubated with 1:2:2 Ac_2O/EtOAc/Collidine (5 mL) for 30 min on synthesizer, then washed with DMF (x3), then washed with DCM (x4), then dried for 20 min. The dry resin was stirred in a round-bottom flask with 2 mL TFA overnight. In the morning, 50 µL TIS and 50 µL H_2O were added until the bright yellow colour disappeared. The TFA is filtered into a 15mL falcon tube, triturated with Et_2O (x3), pellet allowed to dry under air and dissolved in H_2O/MeCN 0.1% FA and purified by HPLC on C18 with gradient elution using 0.1% FA H_2O/MeCN on 50x21mm column. Pure fraction collected, frozen and lyophilized. The pure peptide was re-injected using solvents A: H_2O/0.1% FA and B: MeCN/0.1% FA with an Agilent Eclipse XDDC18 C18 column (9.4x250 mm) eluted

with first 95% H_2O to 65% H_2O with 0.1% FA from 0-32 min, then 65-0% H_2O with 0.1% FA for 32-35 min at a flow rate of 2 mL/min. (t_R = 24.171 min). LRMS-ESI (m/z): $C_{68}H_{98}N_{16}O_{11}S$ $(M+2H)^{2+}/2$ calc 673.4 m/z obs. 673.6 m/z.

[0624] Synthesis of Compound B: From the synthesis of MT16-145-D-Hpi, after the appendage of Fmoc-β-Ala-OH, Fmoc is deprotected by treatment with 20% Piperidine-DMF (3 mL), mixed by N_2 bubbling. Resin is washed with DMF (x3). Fmoc-cysteic acid is coupled and then DOTA at RT using HATU and DIEA in DMF using 4/4/8 equivalents. The dry resin is stirred in a round-bottom flask with 2 mL TFA overnight. In the morning, 50 µL TIS and 50 µL H_2O are added until the bright yellow colour disappeared. The TFA is filtered into a 15 mL falcon tube, triturated with Et_2O (x3), pellet allowed to dry under air.

[0625] Synthesis of BL34N1

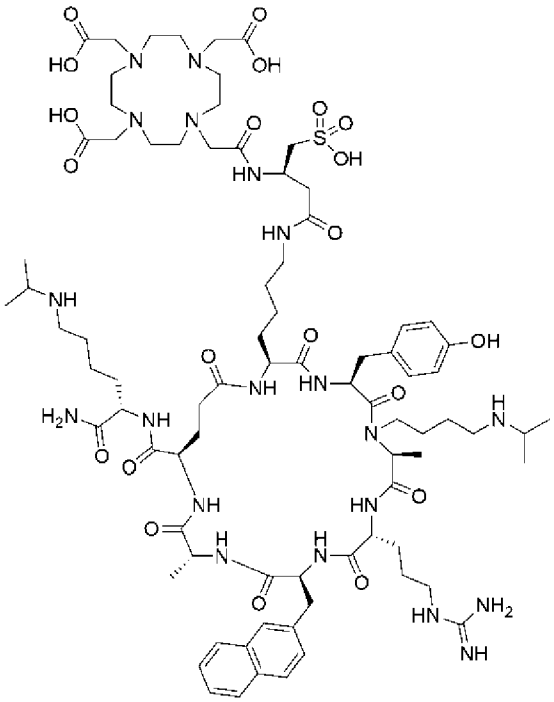


BL34N1

[0626] At a 0.2 mmol scale Fmoc-Rink Amide MBHA resin (Iris GMBH, 0.08 mmol/g) was deprotected with 20% v/v piperidine in DMF for 30 min at RT twice and washed with 3 mL of DMF 7 times. Fmoc-Lys(iPr, Boc)-OH was then conjugated to the resin using 4/8/4 equiv. of Fmoc-AA-OH/DIC/Oxyma in DMF for 1 hr. The resin was washed 7 times with 3 mL DMF after each deprotection. The Fmoc group was removed with 20% v/v piperidine in DMF for 25 min. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), and Fmoc-Lys(iPr, Boc)-OH were sequentially coupled to the peptidyl resin following similar procedures.

[0627] Resin (0.15 mmol) was treated with *o*-nitrobenzenesulfonyl chloride (3 eq.) and 2,4,6-collidine (5 eq.) in CH_2Cl_2 (0.1 M) for 2 h at RT. After the resin was washed (CH_2Cl_2 x3, DMF x3, and THF x3), to a suspension of the N-Ns-protected resin in anhydrous THF (0.1 M) were added MeOH (5 eq.), PPh_3 (5 eq.), and diethyl diazodicarboxylate (5 eq.) at 0°C. The mixture was shaken for 2 h at RT, followed by washing the resin (THF x3 and $CHCl_3$ x3). The N-methylated resin was treated with DBU (5 eq.) and 2-mercaptoethanol (10 eq.) for 1.5 h at RT to give the protected peptide resin having an N-methyl amino acid at the N-terminus. For the coupling of Fmoc amino acid to the N-methyl amino acid, HATU and 1-hydroxy-7-azabenzotriazole (HOAt) were employed. The Fmoc group was deprotected by treatment with 20% (v/v) piperidine-DMF for 20 min. In this case it would be Fmoc-Tyr(tBu)-OH. Fmoc-Lys(ivDde)-OH (x2) was sequentially coupled to the peptidyl resin using 4/8/4 equiv. of Fmoc-AA-OH/DIC/Oxyma in DMF and shaken for 1 hr. The –OAll protecting group on D-Glu was removed using $Pd(PPh_3)_4$ (30 mg)/Phenylsilane (450 µL) in DCM (6 mL) (4 x 25 min at rt). The N^{α}-Fmoc on Lys(ivDde) was then removed, and cyclization was performed using DIC/HOBt in DMF (2 x 2h at rt). Following cyclization, the ivDde group was removed *via* adding 3 mL of 2% N_2H_4 in DMF for 10 minutes, with 4 cycles. Fmoc-cysteic acid was coupled and then $DOTA(tBu)_3$ at RT using HATU and DIEA in DMF using 4/4/8 equivalents. The peptide was deprotected and simultaneously cleaved from the resin by treating with a cocktail solution of 92.5/2.5/2.5 TFA/TIS/H_2O for 5 h at RT. After filtration, the TFA was removed *in vacuo* and the peptide was precipitated by the addition of cold diethyl ether. The crude peptide was purified by semi-preparative HPLC using the semi-preparative column eluted with first 5% MeCN in H_2O with 0.1% TFA for 0-7 min, then 5-35% MeCN for 7-8 min, then 35-100% MeCN in 8-9 min at a flow rate of 15 mL/min (t_R = 5.167 min). $C_{80}H_{126}N_{20}O_{21}S$ Calc mass: $[M+2H]^{2+}/2$: 868.5 m/z; found $[M+2H]^{2+}/2$: 869.0 m/z.

[0628] Synthesis of BL34P1



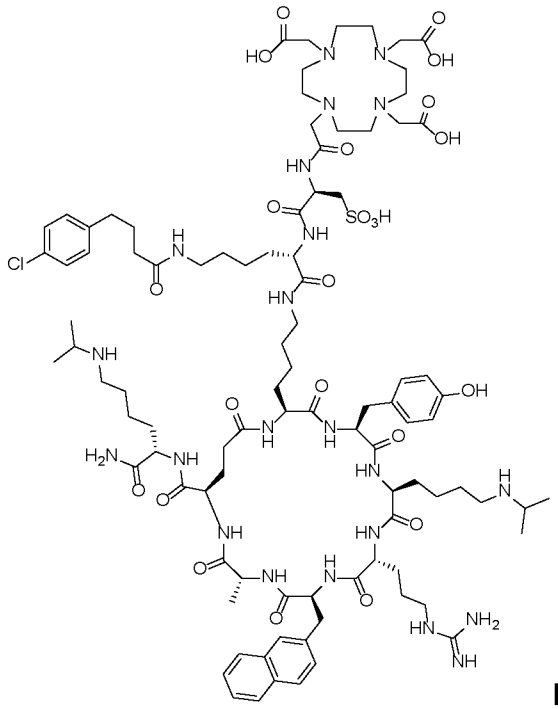
BL34P1

[0629] From the synthesis of BL34N1, following the removal of the Fmoc group of Fmoc-D-Arg-OH at a 0.05 mmol scale, the resin was coupled twice using 4/8/4 equiv. of Fmoc-D-Ala-OH/DIC/Oxyma in DMF for 1 hr at rt. After coupling Fmoc-D-Ala-OH, the Fmoc group was removed with 20% v/v piperidine in DMF for 25 min and the resin washed seven times before treated with *o*-nitrobenzenesulfonyl chloride (3 eq.) and 2,4,6-collidine (5 eq.) in CH_2Cl_2 (0.1 M) for 2 h at RT. After the resin was washed (CH_2Cl_2 x3, DMF x3, and THF x3), to a suspension of the N-Ns-protected resin in anhydrous THF (0.1 M) were added tBu-(4-hydroxybutyl)(isopropyl)carbamate (5 eq.), PPh_3 (5 eq.), and diethyl diazodicarboxylate (5 eq.) at 0°C. The mixture was shaken for 2 h at RT, followed by washing the resin (THF × 3 and $CHCl_3$ × 3). This cycle was repeated three times for complete alkylation. The N-alkylated resin was treated with DBU (5 eq.) and 2-mercaptoethanol (10 eq.) for 1.5 h at RT to give the protected peptide resin having an N-methyl amino acid at the N-terminus. For the coupling of Fmoc amino acid to the N-methyl amino acid, HATU and HOAt were employed. The Fmoc group was deprotected by treatment with 20% (v/v) piperidine-DMF for 20 min. In this case it would be Fmoc-Tyr(tBu)-OH. Fmoc-Lys(ivDde)-OH (x2) was sequentially coupled to the peptidyl resin using 4/8/4 equiv. of Fmoc-AA-OH/DIC/Oxyma in DMF and shaken for 1 hr. The –OAll protecting group on D-Glu was removed using $Pd(PPh_3)_4$ (10 mg)/Phenylsilane (150 µL) in DCM (5 mL) (4 x 25 min at rt). The N^a-Fmoc on Lys(ivDde) was then removed, and cyclization was performed using DIC/HOBt in DMF (2 x 2 h at rt). Following cyclization, the ivDde group was removed *via* adding 3 mL of 2% N_2H_4 in DMF for 10 min, with 4 cycles. Fmoc-cysteic acid-OH was coupled and then $DOTA(tBu)_3$ at RT using HATU and DIEA in DMF using

4/4/8 equivalents. The peptide was deprotected and simultaneously cleaved from the resin by treating with a cocktail solution of 92.5/2.5/2.5 TFA/TIS/H_2O for 5 h at rt. After filtration, the TFA was removed *in vacuo* and the peptide was precipitated by the addition of cold diethyl ether.

[0630] The crude peptide was purified by semi-preparative HPLC using the semi-preparative column eluted with first 5% acetonitrile in water with 0.1% TFA for 0-7 mins, then 5-35% acetonitrile for 7-8 min, then 35-100% acetonitrile in 8-9 min at a flow rate of 15 mL/min (t_R = 5.478 min). ESI-MS: calculated $[M+Na+K]^{2+}/2$ for BL34P1 $C_{81}H_{128}N_{20}O_{21}SNaK$ 906.1 m/z; found $[M+Na+K]^{2+}/2$ 906.6 m/z.

[0631] Synthesis of BL34L16

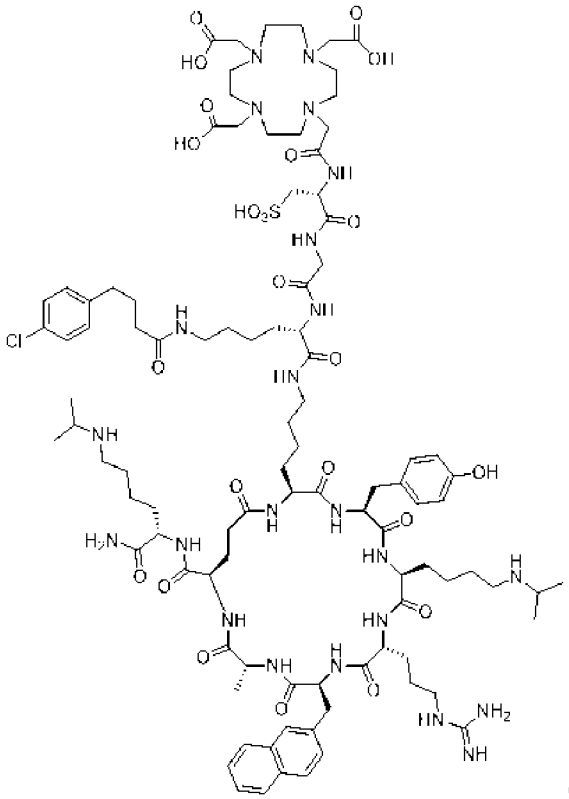


BL34L16

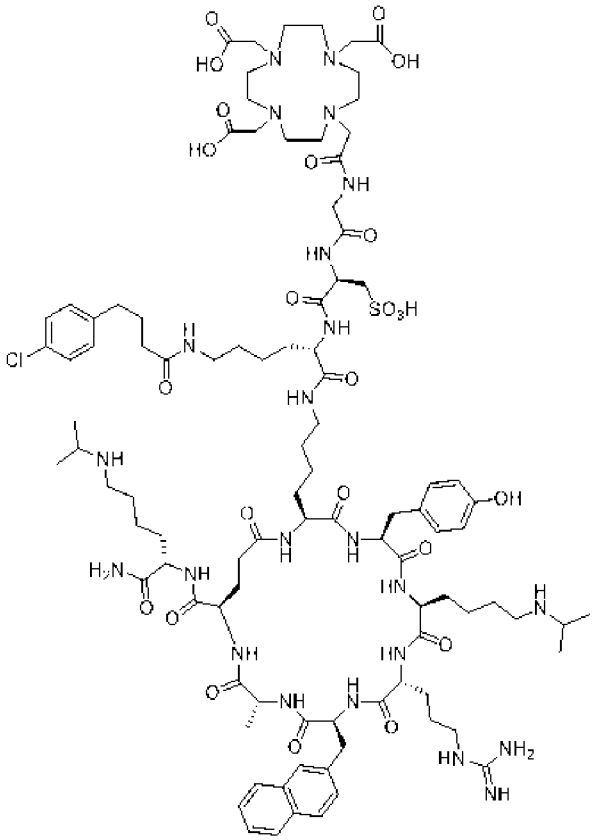
[0632] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x 3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll group was removed with Pd(PPh3)4/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-Lys(ivDde)-OH and Fmoc-cysteic acid were

coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/HOAt/DIPEA (4/4/8 eq.), followed by ivDde deprotection, and 4-(4-chlorophenyl)butanoic acid coupling with HATU/HOAt/DIPEA (4/4/8 eq.). The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/MeCN mixture. The crude peptide was purified with prep HPLC using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 30 mL/min (20%-40% B over 15 min, tR = 7.82 min). The sample was lyophilized to a white solid. Calc mass (M+H+): 2030.03 m/z; found (M + 3H)3+/3: 677.81 m/z.

[0633] Synthesis of Compounds C and D



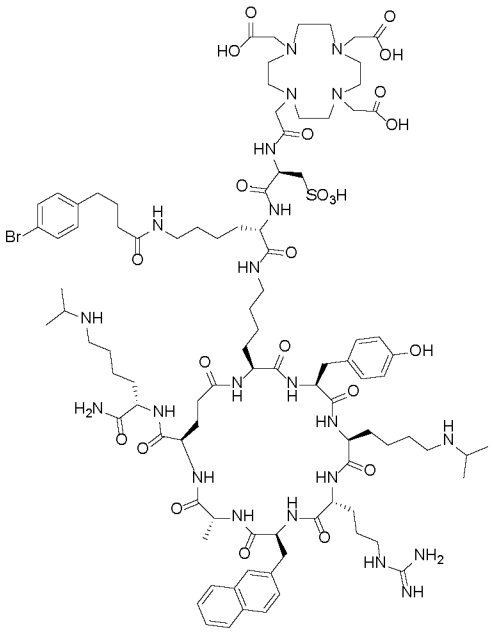
Compound C



Compound D

[0634] Compounds C and D can made according to the exemplary synthetic route outlined above for BL34L16.

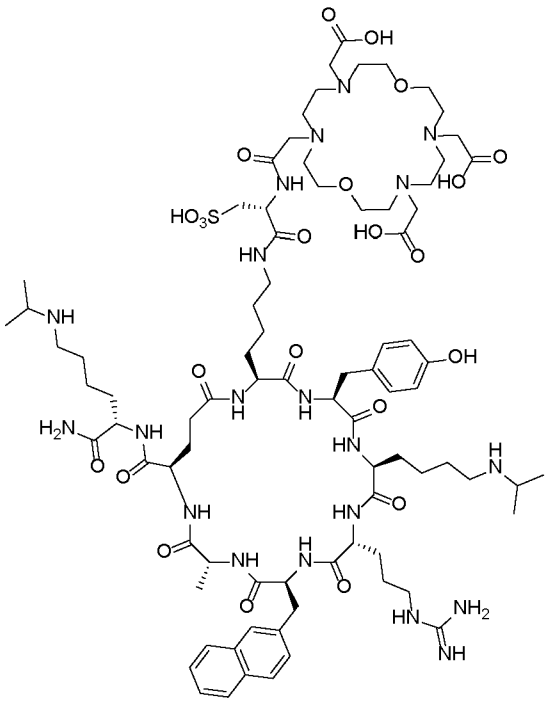
[0635] Synthesis of BL34L20



BL34L20

[0636] At a 0.1 mmol scale, Rink Amide Protide resin was deprotected with 20% Piperidine-DMF (3 mL) at 90°C (1 min), and then washed with DMF (3 mL x 3). Then, Fmoc-Lys(iPr, Boc)-OH (5 eq., 0.5 mmol, 0.2 M in DMF) was coupled at 90°C (4 min) using 1 M DIC/ 1 M Oxyma in DMF (1 mL/ 0.5 mL), followed by Fmoc-deprotection as described above. Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH (x2), Fmoc-2-Nal-OH (x2), Fmoc-D-Arg(Pbf)-OH (x2), Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH (x2) and Fmoc-Lys(ivDde)-OH were coupled consecutively in a similar manner. The -OAll group was removed with Pd(PPh3)4/phenylsilane (0.25/15 eq) (35°C, 6 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (1/1/2 eq.) at 75°C (12 min, x3). The ivDde group was removed with 2% hydrazine in DMF (3 mL, RT, 5 min, x5). Fmoc-Lys(ivDde)-OH and Fmoc-cysteic acid were coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/HOAt/DIPEA (4/4/8 eq.), followed by ivDde deprotection, and 4-(4-bromophenyl)butanoic acid coupling with HATU/HOAt/DIPEA (4/4/8 eq.). The peptide was cleaved from the resin with TFA/TIPs/H_2O/Phenol (90/2.5/2.5/5%) at 35°C for 3 h. The crude peptide was precipitated in cold diethyl ether, washed with ether (x2) and lyophilized in a H_2O/MeCN mixture. The crude peptide was purified with prep HPLC using solvents A: H_2O/0.1% TFA and B: MeCN/0.1% TFA, 30 mL/min (25%-35% B over 15 min, tR = 6.00 min). The sample was lyophilized to a white solid. Calc mass (M+H+): 2073.98 m/z; found (M + 2H)2+/2: 1038.29 m/z.

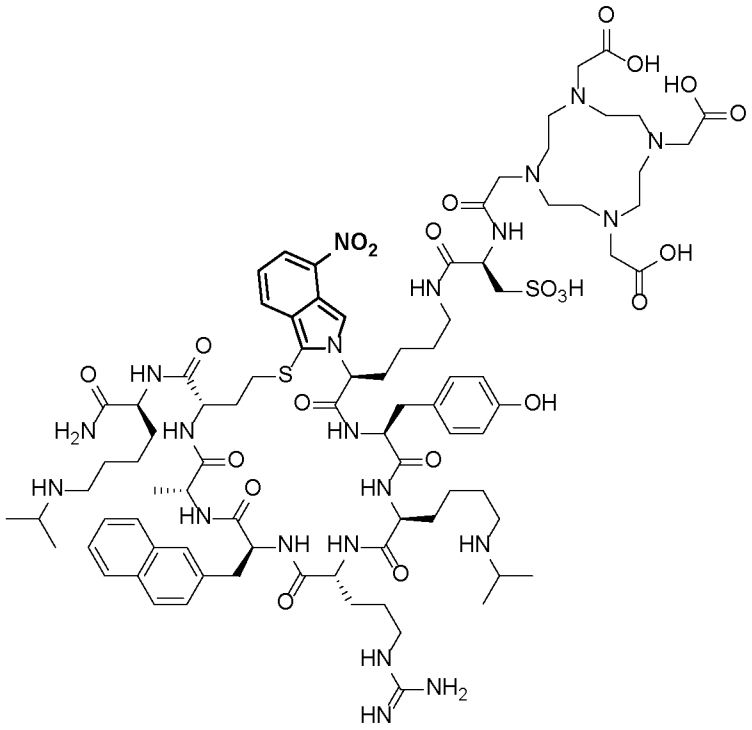
[0637] Synthesis of Crown-BL34



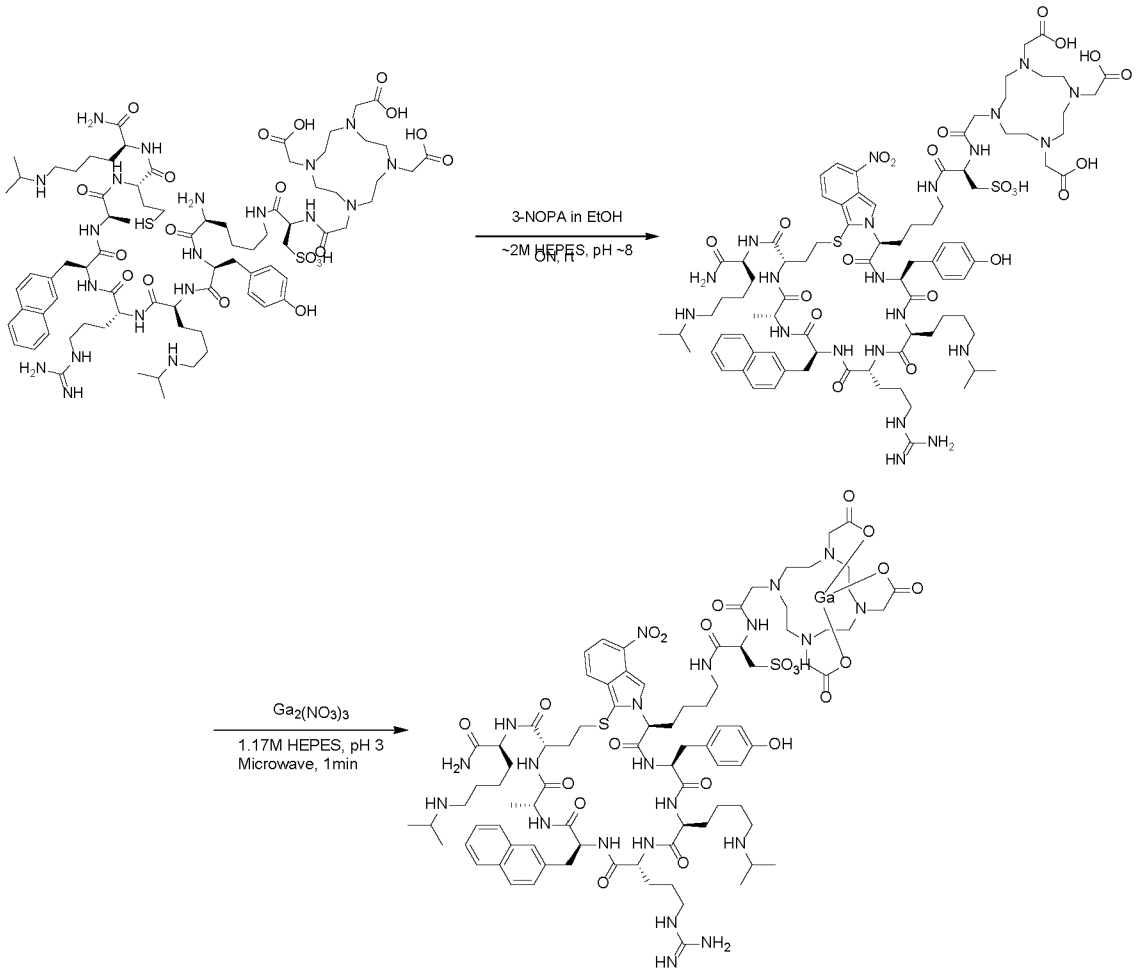
Crown-BL34

[0638] At a 0.05 mmol scale, Rink Amide Protide resin was deprotected by treating the resin with 20% piperidine in DMF (3 × 8 min). Then, Fmoc-Lys(iPr, Boc)-OH was coupled to the resin followed by Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH , Fmoc-2-Nal-OH, Fmoc-D-Arg(Pbf)-OH, Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH and Fmoc-Lys(ivDde)-OH via solid-phase peptide synthesis using Fmoc-based chemistry. All couplings were carried out in DMF using Fmoc-protected amino acid (4 eq.), HATU (4 eq.), and DIEA (7 eq.). The -OAll group was removed with Pd(PPh3)4/phenylsilane (0.25/24 eq) (30 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (3/3/6 eq) and coupled for 12 hr. The ivDde group was removed with 2% hydrazine in DMF (5 x 5 min). Fmoc-cysteic acid was coupled as described above. The synthesis was continued with Crown(tBu)3 (4 eq.) coupling using HATU/DIPEA (4/7 eq). The peptide was then deprotected and simultaneously cleaved from the resin by treating with 95/5 trifluoroacetic acid (TFA)/triisopropylsilane (TIS) for 2 h at room temperature. After filtration, the peptide was precipitated by the addition of cold diethyl ether to the TFA solution. The crude peptide was purified by HPLC using the semi-preparative column. HPLC condition was 13% acetonitrile in trace metal water with 0.1% Formic acid at a flow rate of 4.5 mL/min. The retention time was 9.7 min. The eluates containing the desired peptide were collected, pooled, and lyophilizedthe Calc mass (M+H+): 1809.96 m/z; found $(M + 2H)^{2+}/2$: 905.72 m/z.

[0639] Synthesis of 3NOPA-BL34L2



3NOPA-BL34L2



Scheme: 3-NOPA-BL34L2 Flick Procedure

[0640] Flick and Gallium Chelation: ~2 µmole crude peptide (lyophilized, in a 15mL falcon tube) was dissolved in 400 µL 2M HEPES (pH 9) and 80 µL of 3-NOPA in EtOH Solution (0.05M) was added. Solution was allowed to react overnight at room temperature. Reaction mixture was then acidified with 1M $HCl_{(aq)}$ to pH~4, 300 µL $Ga(NO_2)_3$ in 1M HCl (0.0282M) added (pH ~3) and then transferred to a scintillation vial and heated in a microwave for 1 min at 20% power. Entire reaction mixture was then directly purified by RP-HPLC usings Method A (below).

[0641] Flick only: 4 µmole of pure peptide dissolved in 1mL Borate Buffer (pH ~9.5), 120uL of 0.05M 3-NOPA in EtOH solution added, reaction vortexed and allowed to react at room temperature for 4 hours. 10 µL of formic acid was then added, and the entire reaction mixture was purified directly by RP-HPLC using Method A.

[0642] Pure peptide reinjection:

[0643] LRMS ($C_{86}H_{124}GaN_{21}O_{22}S_2$): $(M+2H)^{2+/2}$ Observed: 969.8, Calculated: 969.4 (For 1 ^{13}C)

[0644] HPLC Retention Time: (Method A) 27.6min

[0645] Method A: 15mL/min 50x21mm C18 Solvent A: 0.1% Formic Acid H_2O Solvent B: 0.1% Formic Acid MeCN

[0646] 0-7.5min 95:5 A/B - 65:35 A/B

[0647] 7.5min-8.0min 65:35 A/B - 0:1 A/B

[0648] 8.0min-9.5min 0:1 A/B

[0649] HPLC Method B: 2mL/min 9.4x250mm C18 Solvent A: 0.1% Formic Acid H_2O, Solvent B: 0.1% Formic Acid MeCN.

[0650] 0-12min 80:20 A/B - 60:40 A/B

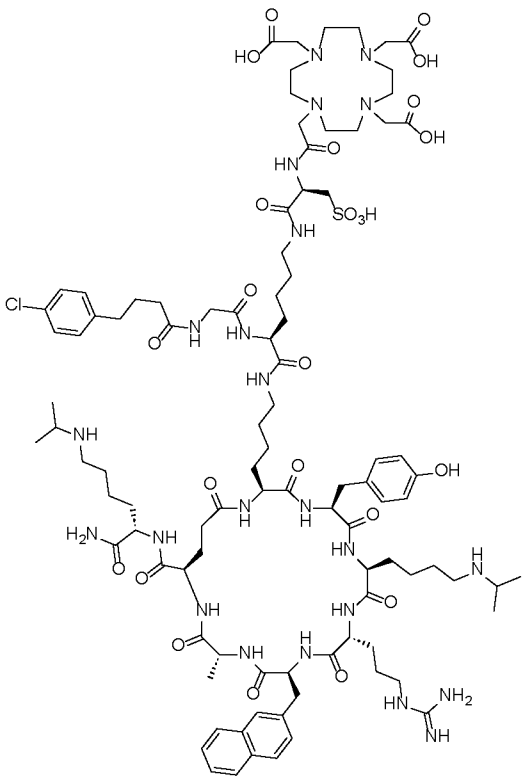
[0651] 12min-15min 60:40 A/B - 0:1 A/B

[0652] 15min-20min 0:1 A/B

[0653] 20min-23min 0:1 A/B - 80:20 A/B

[0654] 23min-29min 80:20 A/B

[0655] Synthesis of BL34T1

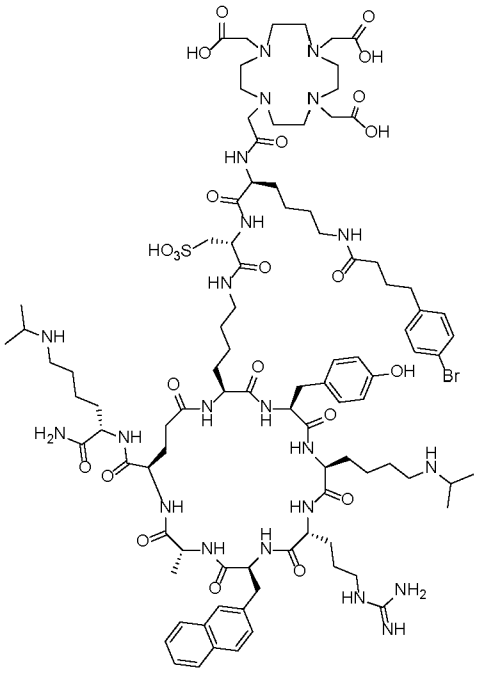


BL34T1

[0656] At a 0.05 mmol scale, Rink Amide Protide resin was deprotected by treating the resin with 20% piperidine in DMF (3 × 8 min). Then, Fmoc-Lys(iPr, Boc)-OH was coupled to the resin followed by Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH , Fmoc-2-Nal-OH, Fmoc-D-Arg(Pbf)-OH, Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH and Fmoc-Lys(ivDde)-OH via solid-phase peptide synthesis using Fmoc-based chemistry. All couplings were carried out in

DMF using Fmoc-protected amino acid (4 eq.), HATU (4 eq.), and DIEA (7 eq.). The -OAll group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/24 eq) (30 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (3/3/6 eq) and coupled for 12 hr. The ivDde group was removed with 2% hydrazine in DMF (5 x 5 min). Fmoc-Lys(ivDde)-OH, Fmoc-GlyOH and *p*-chloro 4-phenylbutyric acid were subsequently coupled to the sequence as described above. After selective removal of the ivDde-protecting group with 2% hydrazine in DMF (5 × 5 min), Fmoc-cysteic acid was then coupled to the Lys side chain. The synthesis was continued with $Crown(tBu)_3$ (4 eq.) coupling using HATU/DIPEA (4/7 eq). The peptide was then deprotected and simultaneously cleaved from the resin by treating with 95/5 trifluoroacetic acid (TFA)/triisopropylsilane (TIS) for 2 h at room temperature. After filtration, the peptide was precipitated by the addition of cold diethyl ether to the TFA solution. The crude peptide was purified by HPLC using the semi-preparative column. HPLC condition was 28% acetonitrile with 0.1% TFA at a flow rate of 4.5 mL/min. The retention time was 12.7 min. The eluates containing the desired peptide were collected, pooled, and lyophilized. Calc mass $(M+2H)^{2+}/2$: 1044.0 m/z; found $(M + 2H)^{2+}/2$: 1044.0 m/z.

[0657] Synthesis of BL34L20S



BL34L20S

[0658] At a 0.05 mmol scale, Rink Amide Protide resin was deprotected by treating the resin with 20% piperidine in DMF (3 × 8 min). Then, Fmoc-Lys(iPr, Boc)-OH was coupled to the resin followed by Fmoc-D-Glu(OAll)-OH, Fmoc-D-Ala-OH , Fmoc-2-Nal-OH, Fmoc-D-Arg(Pbf)-OH, Fmoc-Lys(iPr, Boc)-OH, Fmoc-Tyr(tBu)-OH and Fmoc-Lys(ivDde)-OH via

solid-phase peptide synthesis using Fmoc-based chemistry. All couplings were carried out in DMF using Fmoc-protected amino acid (4 eq.), HATU (4 eq.), and DIEA (7 eq.). The -OAll group was removed with $Pd(PPh_3)_4$/phenylsilane (0.25/24 eq) (30 min, x2), followed by Fmoc-deprotection. Cyclization was performed with HATU/HOAt/DIPEA (3/3/6 eq) and coupled for 12 hr. The ivDde group was removed with 2% hydrazine in DMF (5 x 5 min). Fmoc-cysteic acid and Fmoc-Lys(ivDde)-OH were then coupled as described above. The synthesis was continued with DOTA (4 eq.) coupling using HATU/DIPEA (4/7 eq.), followed by ivDde deprotection, and 4-(4-bromophenyl)butanoic acid coupling with HATU/DIPEA (4/7 eq.). The peptide was then deprotected and simultaneously cleaved from the resin by treating with 95/5 trifluoroacetic acid (TFA)/triisopropylsilane (TIS) for 2 h at room temperature. After filtration, the peptide was precipitated by the addition of cold diethyl ether to the TFA solution. The crude peptide was purified by HPLC using the semi-preparative column. HPLC condition was 29% acetonitrile with 0.1% TFA at a flow rate of 4.5 mL/min. The retention time was 13.2 min. The eluates containing the desired peptide were collected, pooled, and lyophilized. Calc mass $(M+2H)^{2+}/2$: 1037.5 m/z; found $(M + 2H)^{2+}/2$: 1038.0 m/z.

Activity Data

[0659] Cell Culture

[0660] The Z138 Mantle cell lymphoma cell line was purchased from the American Type Culture Collection (ATCC®CRL-3001). The cell line was cultured in a 5% CO_2 atmosphere at 37°C in a humidified incubator with IMDM medium supplemented with 10% fetal bovine serum, 100 I.U./mL penicillin, and 100 µg/mL streptomycin.

[0661] Competitive Binding Assay

[0662] CHO:CXCR4 cells were seeded at a density of 1×10^5 cells/well in 24-well poly-D-lysine coated plates (Corning BioCoat) and incubated with [^{125}I]SDF-1α (0.01 nM, PerkinElmer) and competing nonradioactive ligands (1 µM to 0.1 pM). The cells, radioligand, and competing peptides were incubated for 1 h at 27 °C with moderate shaking. Following the incubation period, the supernatant was aspirated, followed by three washes with 1 mL of ice-cold PBS. Cells were harvested with 200 µL of trypsin and counted on a γ counter. Data were plotted in GraphPad Prism 7 to determine IC_{50} values (GraphPad Software, Inc., La Jolla, CA). The values are reported as mean ± standard deviation. Results for a subset of compounds are shown in Table 7.

[0663] Radiolabeling

[0664] [^{68}Ga]$GaCl_3$ was eluted from an iThemba Labs generator with a total of 4 mL of 0.1 M HCl. The eluted [^{68}Ga]$GaCl_3$ solution was added to 2 mL of concentrated HCl. This radioactive mixture was then added to a DGA resin column and washed with 3 mL of 5 M HCl. The column

was then dried with air and the [^{68}Ga]$GaCl_3$ (0.10 – 0.50 GBq) was eluted with 0.5 mL of water into a vial containing a solution of the unlabeled precursor (25 µg) in 0.7 mL HEPES buffer (2 M, pH 5.3). The reaction mixture was heated in a microwave oven (Danby; DMW7700WDB) for 1 min at power setting 2. The mixture was purified by semi-prep HPLC and quality control was performed via analytical HPLC with the co-injection of the unlabeled standard with a one-twelfth of the radiotracer. Radiochemical yields (decay-corrected) were >50% and radiochemical purities were >95%.

[0665] Animal Models

[0666] Animal experiments were performed in accordance with guidelines established by the Canadian Council on Animal Care, under a research protocol approved by the Animal Ethics Committee of the University of British Columbia. For all studies, male NOD.Cg-Rag1tm1MomIl2rgtm1Wjl/SzJ (NRG) mice were used and cells injected in a 100 µL solution of 1:1 ratio of PBS/Matrigel. For preclinical imaging and biodistribution studies, 5×10^6 cells of Z138, cells were subcutaneously inoculated on the left or right flank and tumors were grown to a size of 200-300 mm^3.

[0667] PET/CT imaging

[0668] PET/CT imaging experiments were conducted using a Siemens Inveon small-animal PET/CT scanner. Each tumor-bearing mouse was injected with about 6–8 MBq of ^{68}Ga-labeled tracer through a lateral caudal tail vein. After 50 min after injection, a 10-min CT scan was conducted first for localization and attenuation correction after segmentation for reconstructing the PET images; this scan was followed by a 10-min static PET acquisition.

[0669] Radiolabeling with ^{177}Lu

[0670] For compounds conjugated to DOTA chelator, [^{177}Lu]$LuCl_3$ (740-925 MBq) was added to a solution of precursor (10 nmole) in sodium acetate buffer (0.5 mL, 0.1 M, pH 4.5). The mixture was incubated at 90°C for 15 min, and then purified by HPLC using the semi-preparative column. For compounds conjugated to Crown chelator, [^{177}Lu]$LuCl_3$ (810 MBq) was added to a solution of precursor (10 nmole) in ammonia acetate buffer (0.5 mL, 0.1 M, pH 5.5) with 10% ethanol. The mixture was incubated at 37°C for 30 min, and then purified by HPLC using the semi-preparative column. The eluate fraction containing the radiolabeled product was collected, diluted with water (50 mL), and passed through a C18 Sep-Pak cartridge that was pre-washed with ethanol (1 mL) and water (1 mL x 2). The ^{177}Lu-labeled product was eluted off the cartridge with ethanol (0.4 mL) and diluted with saline in 1% ascorbate for imaging and biodistribution. Quality control and the co-injection of the natLu-labeled standard with the radiotracer were performed using the analytical column.

[0671] SPECT/CT imaging

[0672] SPECT/CT imaging experiments were conducted using the MILabs U-SPECT-II/CT scanner. The tumor-bearing mouse was injected with about 18.5-37 MBq of ^{177}Lu-labeled

compound through a lateral caudal tail vein. The mice were imaged at 1, 4, 24, 72, and 120 h after injection. At each time point, a 5-min CT scan was conducted first for anatomic reference; afterward, two 30-min static emission scans were acquired in list mode. Results for the following subset of compounds: [^{68}Ga]Ga-BL34L11, [^{177}Lu]Lu-BL34L11, and [^{177}Lu]Lu-BL34L20, [^{177}Lu]Lu-crown-BL34, [^{68}Ga]Ga-BL34N1, [^{68}Ga]Ga-BL34T1, [^{177}Lu]Lu-BL34T1, and [^{177}Lu]Lu-BL34L20S are shown at **FIGs. 1-8**, respectively.

[0673] Biodistribution

[0674] Under isoflurane anesthesia (2-2.5% isoflurane in 2L/min O_2), mice were injected intravenously with [^{68}Ga]Ga-BL34L6 or [^{68}Ga]Ga-BL34L7. Mice were euthanized by CO_2 inhalation after anesthesia with isoflurane. Tissues were harvested, washed in PBS, patted dry, weighed, and then assayed radioactivity on a gamma counter. Counted radioactivities were converted to percentage injected dose per gram of tissue (%ID/g) using a calibration curve. Results for a subset of compounds are shown in Tables 8-17.

[0675] Table 7: Binding affinity of BL34L6, BL34L7, and BL34L8 for hCXCR4

Peptide	IC_{50} (nM)
BL34L6	10-50
BL34L7	10-50
BL34L8	>100

[0676] Table 8: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34L6 in Z138 tumor-bearing mice at 1 h (p.i.)

[68Ga]Ga-BL34L6	1 h		
	Mean	SD	n
Blood	0.83	0.37	4
Testes	0.26	0.10	4
Stomach	0.05	0.01	4
Small Intestine	0.24	0.09	4
Spleen	0.45	0.17	4
Pancreas	0.12	0.04	4
Liver	1.60	0.49	4
Adrenals	0.29	0.15	4
Kidneys	2.07	0.54	4
Lungs	0.99	0.51	4
Heart	0.22	0.07	4
Muscle	0.12	0.06	4
Bone	0.14	0.04	4
Brain	0.01	0.00	4
Z138 Tumor	8.92	2.36	4
Ratios			
Tumor-to-Blood	11.55	2.91	4

[68Ga]Ga-BL34L6	1 h		
	Mean	SD	n
Tumor-to-Muscle	84.57	31.12	4
Tumor-to-Kidney	4.36	0.62	4
Tumor-to-Pancreas	75.31	17.14	4
Tumor-to-Bone	66.48	12.82	4

[0677] Table 9: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34L7 in Z138 tumor-bearing mice at 1 h (p.i.)

[^{68}Ga]Ga-BL34L7	1 h		
	Mean	SD	n
Blood	1.73	0.44	4
Testes	0.44	0.14	4
Stomach	0.09	0.01	4
Small Intestine	0.34	0.06	4
Spleen	0.59	0.18	4
Pancreas	0.23	0.05	4
Liver	1.24	0.32	4
Adrenals	0.52	0.31	4
Kidneys	2.45	0.44	4
Lungs	1.75	0.91	4
Heart	0.41	0.14	4
Muscle	0.14	0.04	4
Bone	0.40	0.32	4
Brain	0.04	0.01	3
Z138 Tumor	11.09	2.15	4
Ratios			
Tumor-to-Blood	6.50	0.40	4
Tumor-to-Muscle	87.08	38.47	4
Tumor-to-Kidney	4.51	0.12	4
Tumor-to-Pancreas	9.07	0.70	4
Tumor-to-Bone	37.21	17.44	4

[0678] Table 10: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34L11 in Z138 tumor-bearing mice at 1 h and 3 h (p.i.)

[^{68}Ga]Ga-BL34L11	1 h			3h		
	Mean	SD	n	Mean	SD	n
Blood	18.70	1.61	4	13.44	1.17	5
Testes	2.14	0.47	4	2.59	0.14	5
Stomach	0.97	0.73	4	0.48	0.19	5
Small Intestine	1.28	0.62	4	1.11	0.08	5
Spleen	2.35	0.16	4	2.00	0.48	5
Pancreas	1.67	0.19	4	1.42	0.12	5

[^{68}Ga]Ga-BL34L11	1 h			3h		
	Mean	SD	n	Mean	SD	n
Liver	3.70	0.30	4	3.02	0.38	5
Adrenals	4.99	3.37	4	2.34	1.17	5
Kidneys	5.39	1.14	4	3.90	0.43	5
Lungs	8.36	1.27	4	6.64	0.92	5
Heart	4.53	0.47	4	3.17	0.41	5
Muscle	1.39	0.20	4	1.08	0.05	5
Bone	1.53	0.40	4	1.23	0.37	5
Brain	0.29	0.04	4	0.22	0.02	5
Z138 Tumor	6.55	1.52	4	11.31	1.56	5
Ratios						
Tumor-to-Blood	0.35	0.09	4	0.85	0.15	5
Tumor-to-Muscle	4.85	1.67	4	10.51	1.51	5
Tumor-to-Kidney	1.27	0.45	4	2.91	0.42	5
Tumor-to-Pancreas	3.91	0.73	4	7.95	0.80	5
Tumor-to-Bone	4.32	0.38	4	10.33	4.93	5

[0679] Table 11: Biodistribution data (%ID/g) of [^{177}Lu]Lu-BL34L11 in Z138 tumor-bearing mice at 1 h, 3 h, 24 h, 72 h, and 120 h (p.i.)

[^{177}Lu]Lu-BL34L11	1 h			3h			24 h			72 h			120 h		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Blood	18.59	2.84	8	14.23	2.99	8	7.82	0.95	8	2.84	0.33	8	1.60	0.20	7
Testes	2.49	0.63	8	3.53	0.85	8	2.64	0.59	8	1.47	1.08	8	2.04	0.23	7
Stomach	0.61	0.24	8	0.83	0.30	8	0.75	0.36	8	0.32	0.09	8	0.24	0.05	7
Small Intestine	1.56	0.30	8	1.35	0.36	8	0.79	0.22	8	0.38	0.05	8	0.21	0.05	7
Spleen	1.56	0.30	8	2.03	0.54	8	2.13	0.44	8	1.96	0.41	8	1.86	0.41	7
Pancreas	1.80	0.34	8	1.54	0.39	8	1.05	0.09	8	0.45	0.11	8	0.53	0.31	7
Liver	3.14	0.62	8	3.18	0.74	8	1.99	0.14	8	1.10	0.18	8	0.45	0.12	7
Adrenals	3.76	0.81	8	3.12	1.55	8	2.44	0.94	8	1.80	0.62	8	1.62	0.62	7
Kidneys	5.23	0.80	8	3.92	0.82	8	2.67	0.38	8	1.19	0.13	8	0.75	0.10	7
Lungs	14.83	5.82	8	7.95	2.85	8	4.88	1.29	8	2.86	0.67	8	1.91	0.41	7
Heart	4.23	0.62	8	3.34	0.54	8	1.80	0.77	8	1.10	0.14	8	0.76	0.15	7
Muscle	1.20	0.20	8	1.25	0.22	8	0.76	0.12	8	0.38	0.05	8	0.21	0.04	7
Bone	1.16	0.29	8	0.97	0.39	8	0.71	0.28	8	0.42	0.12	8	0.29	0.10	7
Brain	0.29	0.05	8	0.22	0.05	8	0.18	0.05	8	0.07	0.01	8	0.05	0.01	7
Z138 Tumor	4.09	1.56	8	9.81	2.13	8	26.60	4.91	8	35.03	5.31	8	41.23	18.18	7
Ratios															
Tumor-to-Blood	0.22	0.05	8	0.69	0.11	8	3.42	0.56	8	12.31	1.06	8	24.97	9.12	7

[^{177}Lu]Lu-BL34L11	1 h			3h			24 h			72 h			120 h		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Tumor-to-Muscle	3.35	0.80	8	7.89	1.20	8	35.82	9.79	8	91.84	8.20	8	189.63	60.05	7
Tumor-to-Kidney	0.78	0.22	8	2.52	0.37	8	10.08	1.89	8	29.32	2.88	8	54.25	23.16	7
Tumor-to-Pancreas	2.31	0.78	8	6.59	1.67	8	25.85	6.69	8	71.68	8.43	8	122.17	50.99	7
Tumor-to-Bone	2.39	1.55	8	8.14	10.00	8	28.27	30.56	8	53.72	69.32	8	55.86	70.90	7

[0680] Table 12: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34L16 in Z138 tumor-bearing mice at 1 h and 3 h (p.i.)

[^{68}Ga]Ga-BL34L16	1 h			3h		
	Mean	SD	n	Mean	SD	n
Blood	7.27	0.99	4	2.70	0.65	5
Testes	1.16	0.57	4	0.68	0.13	5
Stomach	0.26	0.05	4	0.16	0.05	5
Small Intestine	0.86	0.19	4	0.41	0.07	5
Spleen	2.48	1.94	4	2.05	1.65	5
Pancreas	0.76	0.19	4	0.31	0.07	5
Liver	2.61	1.01	4	2.33	1.04	5
Adrenals	1.63	0.50	4	0.70	0.20	5
Kidneys	3.56	0.57	4	2.20	0.30	5
Lungs	5.90	1.46	4	2.85	0.90	5
Heart	1.66	0.22	4	0.67	0.20	5
Muscle	0.61	0.14	4	0.32	0.07	5
Bone	2.65	2.06	4	2.01	1.37	5
Brain	0.11	0.01	4	0.06	0.01	5
Z138 Tumor	10.08	2.02	4	15.23	2.15	5
Ratios						
Tumor-to-Blood	1.38	0.18	4	5.74	0.56	5
Tumor-to-Muscle	16.78	2.79	4	50.43	15.51	5
Tumor-to-Kidney	2.83	0.36	4	6.92	0.21	5
Tumor-to-Pancreas	13.55	1.88	4	50.69	4.69	5
Tumor-to-Bone	6.11	4.03	4	19.26	26.50	5

[0681] Table 13: Biodistribution data (%ID/g) of [^{177}Lu]Lu-BL34L20 in Z138 tumor-bearing mice at 1 h, 3 h, 24 h, 72 h, and 120 h (p.i.)

[^{177}Lu]Lu-BL34L20	1 h			3h			24 h			72 h			120 h		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Blood	14.07	1.59	8	11.84	0.81	8	2.84	0.52	8	0.45	0.10	8	0.36	0.09	9
Testes	1.78	0.30	8	2.81	0.42	8	1.01	0.37	8	0.65	0.14	8	0.56	0.11	9
Stomach	0.52	0.12	8	0.71	0.20	8	0.41	0.09	8	0.13	0.07	8	0.07	0.02	9
Small Intestine	1.16	0.05	8	1.02	0.14	8	0.53	0.24	8	0.11	0.03	8	0.08	0.02	9
Spleen	1.92	0.29	8	1.86	0.25	8	1.12	0.21	8	0.95	0.34	8	0.77	0.20	9
Pancreas	1.59	0.20	8	1.25	0.20	8	1.38	0.28	8	0.12	0.04	8	0.23	0.13	9
Liver	2.80	0.34	8	3.16	0.42	8	0.84	0.52	8	0.44	0.15	8	0.19	0.12	9
Adrenals	2.44	1.49	8	2.29	0.73	8	1.10	0.76	8	0.81	0.39	8	1.24	2.08	9
Kidneys	4.50	0.48	8	3.98	0.47	8	1.53	0.22	8	0.40	0.09	8	0.33	0.07	9
Lungs	8.78	0.84	8	6.60	1.04	8	1.90	0.27	8	0.68	0.17	8	0.72	0.64	9
Heart	3.05	0.33	8	3.01	0.18	8	0.76	0.33	8	0.25	0.04	8	0.18	0.04	9
Muscle	1.13	0.07	8	0.93	0.07	8	0.27	0.03	8	0.15	0.13	8	0.08	0.03	9
Bone	1.02	0.25	8	0.78	0.20	8	0.29	0.09	8	0.26	0.17	8	0.30	0.23	9
Brain	0.22	0.02	8	0.20	0.04	8	0.06	0.01	8	0.03	0.02	8	0.02	0.01	9
Z138 Tumor	5.94	1.20	8	15.38	2.37	8	27.38	6.03	8	23.65	5.21	8	23.59	9.39	9
Ratios															
Tumor-to-Blood	0.42	0.08	8	1.30	0.15	8	9.65	1.60	8	53.94	8.13	8	71.48	40.82	9
Tumor-to-Muscle	5.29	1.14	8	16.67	2.76	8	101.97	15.64	8	233.96	116.23	8	356.88	210.38	9
Tumor-to-Kidney	1.32	0.23	8	3.93	0.82	8	17.99	3.98	8	60.33	11.41	8	75.48	34.84	9
Tumor-to-Pancreas	3.77	0.83	8	12.58	2.60	8	70.90	13.72	8	206.32	40.30	8	257.05	140.78	9
Tumor-to-Bone	3.63	3.06	8	10.47	10.86	8	45.34	49.49	8	44.26	49.86	8	27.03	36.72	9

[0682] Table 14: Biodistribution data (%ID/g) of [^{68}Ga]Ga-3NOPA-BL34L2 in Z138 tumor-bearing mice at 1 h (p.i.)

[^{68}Ga]Ga-3NOPA-BL34L2	1 h		
	Mean	SD	n
Blood	0.77	0.05	3
Testes	0.33	0.10	3
Stomach	0.12	0.05	3
Small Intestine	0.58	0.08	3
Spleen	2.44	0.38	3
Pancreas	0.21	0.03	3
Liver	12.48	0.55	3
Adrenals	0.70	0.18	3
Kidneys	5.66	0.38	3

[^{68}Ga]Ga-3NOPA-BL34L2	1 h		
	Mean	SD	n
Lungs	4.14	2.02	3
Heart	0.45	0.19	3
Muscle	0.19	0.01	3
Bone	0.56	0.20	3
Brain	0.03	0.00	3
Z138 Tumor	7.97	0.54	3
Ratios			
Tumor-to-Blood	10.41	1.09	3
Tumor-to-Muscle	41.84	1.11	3
Tumor-to-Kidney	1.41	0.17	3
Tumor-to-Pancreas	38.10	6.99	3
Tumor-to-Bone	15.53	5.65	3

[0683] Table 15: Biodistribution data (%ID/g) of [^{177}Lu]Lu-crown-BL34 in Z138 tumor-bearing mice at 1 h, 3 h, 24 h, 72 h, and 120 h (p.i.)

[^{177}Lu]Lu-crown-BL34L20	1 h			3h			24 h			72 h			120 h		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Blood	0.35	0.04	5	0.08	0.01	6	0.02	0.01	6	0.01	0.00	5	0.00	0.00	4
Testes	0.11	0.02	5	0.04	0.00	6	0.04	0.01	6	0.03	0.01	5	0.03	0.01	4
Stomach	0.08	0.03	5	0.09	0.07	6	0.52	0.78	6	0.12	0.05	5	0.14	0.17	4
Small Intestine	0.23	0.03	5	0.10	0.06	6	0.17	0.15	6	0.08	0.03	5	0.06	0.05	4
Spleen	0.29	0.04	5	0.23	0.11	6	0.26	0.04	6	0.24	0.09	5	0.22	0.01	4
Pancreas	0.12	0.08	5	0.04	0.01	6	0.04	0.01	6	0.03	0.01	5	0.03	0.01	4
Liver	0.73	0.04	5	0.77	0.11	6	0.81	0.13	6	0.67	0.12	5	0.59	0.10	4
Adrenals	0.20	0.07	5	0.11	0.03	6	0.10	0.03	6	0.08	0.04	5	0.05	0.02	4
Kidneys	3.02	0.29	5	2.45	0.19	6	1.81	0.21	6	0.94	0.13	5	0.59	0.07	4
Lungs	0.53	0.06	5	0.28	0.09	6	0.20	0.05	6	0.17	0.06	5	0.15	0.04	4
Heart	0.14	0.03	5	0.06	0.01	6	0.05	0.02	6	0.05	0.01	5	0.05	0.01	4
Muscle	0.09	0.04	5	0.03	0.01	6	0.03	0.02	6	0.02	0.01	5	0.01	0.00	4
Bone	0.15	0.03	5	0.15	0.05	6	0.51	0.18	6	0.66	0.16	5	0.56	0.24	4
Brain	0.01	0.00	5	0.01	0.00	6	0.01	0.00	6	0.01	0.00	5	0.00	0.00	4
Z138 Tumor	13.66	1.12	5	11.71	0.91	6	7.28	1.14	6	3.47	0.48	5	2.38	0.30	4
Ratios															
Tumor-to-Blood	39.37	2.89	5	146.52	24.33	6	301.45	63.41	6	396.35	119.01	5	606.54	260.33	4
Tumor-to-Muscle	161.45	48.94	5	429.51	114.75	6	280.73	132.04	6	175.09	62.98	5	177.51	44.59	4

[^{177}Lu]Lu-crown-BL34L20	1 h			3h			24 h			72 h			120 h		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Tumor-to-Kidney	4.54	0.30	5	4.78	0.14	6	4.01	0.25	6	3.69	0.11	5	4.10	0.77	4
Tumor-to-Pancreas	140.13	51.79	5	275.94	50.95	6	198.39	14.48	6	103.04	19.81	5	77.98	15.75	4
Tumor-to-Bone	94.00	17.25	5	83.21	21.28	6	15.27	4.11	6	5.53	1.47	5	5.33	3.61	4

[0684] Table 16: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34N1 in Z138 tumor-bearing mice at 1 h (p.i.)

[^{68}Ga]Ga-BL34N1	1 h		
	Mean	SD	n
Blood	0.32	0.04	5
Testes	0.18	0.08	5
Stomach	0.05	0.02	5
Small Intestine	0.19	0.02	5
Spleen	0.26	0.02	5
Pancreas	0.08	0.01	5
Liver	0.71	0.05	5
Adrenals	0.17	0.02	5
Kidneys	2.70	0.59	5
Lungs	0.44	0.06	5
Heart	0.12	0.01	5
Muscle	0.09	0.05	5
Bone	0.13	0.02	5
Brain	0.02	0.00	5
Z138 Tumor	11.96	1.04	5
Ratios			
Tumor-to-Blood	37.70	3.76	5
Tumor-to-Muscle	156.75	58.2	5
Tumor-to-Kidney	4.60	1.05	5
Tumor-to-Pancreas	145.97	12.13	5
Tumor-to-Bone	92.20	21.57	5

[0685] Table 17: Biodistribution data (%ID/g) of [^{68}Ga]Ga-BL34T1 in Z138 tumor-bearing mice at 1 h and 3h (p.i.)

[68Ga]Ga-BL34T1	1 h			3 h		
	Mean	SD	n	Mean	SD	n
Blood	13.31	1.79	5	7.55	1.13	5
Testes	1.95	0.26	5	1.71	0.24	5
Stomach	0.49	0.15	5	0.44	0.16	5
Small Intestine	1.31	0.20	5	0.89	0.14	5
Spleen	2.30	0.40	5	2.08	0.61	5
Pancreas	1.24	0.20	5	0.92	0.12	5
Liver	2.90	0.27	5	3.02	0.56	5
Adrenals	2.62	0.89	5	1.93	0.43	5
Kidneys	5.01	0.96	5	4.15	0.66	5
Lungs	9.23	2.86	5	5.90	1.13	5
Heart	3.11	0.49	5	1.91	0.35	5
Muscle	0.99	0.18	5	0.73	0.09	5
Bone	1.04	0.40	5	1.28	0.78	5
Brain	0.19	0.03	5	0.16	0.03	5
Z138 Tumor	12.19	1.55	5	23.67	1.92	5
Tumor-to-Blood	0.93	0.19	5	3.17	0.25	5
Tumor-to-Muscle	12.85	3.48	5	32.58	1.97	5
Tumor-to-Kidney	2.52	0.63	5	5.78	0.67	5
Tumor-to-Pancreas	10.12	2.42	5	25.98	2.10	5
Tumor-to-Bone	12.68	3.70	5	21.94	7.02	5

[0686] INCORPORATION BY REFERENCE

[0687] All references, articles, publications, patents, patent publications, and patent applications cited herein are incorporated by reference in their entireties for all purposes. However, mention of any reference, article, publication, patent, patent publication, and patent application cited herein is not, and should not be taken as acknowledgment or any form of suggestion that they constitute valid prior art or form part of the common general knowledge in any country in the world.

[0688] REFERENCES

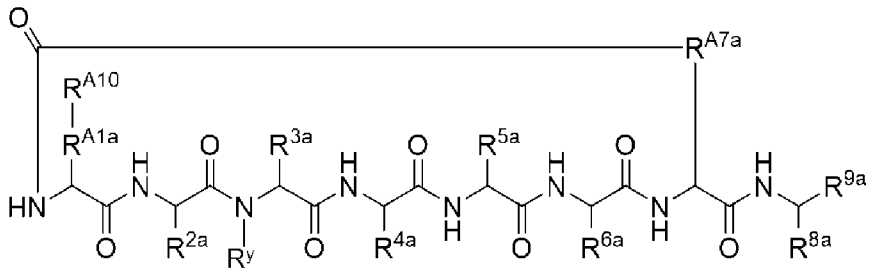
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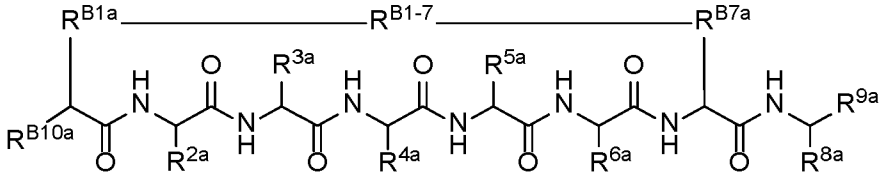
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What is Claimed is:

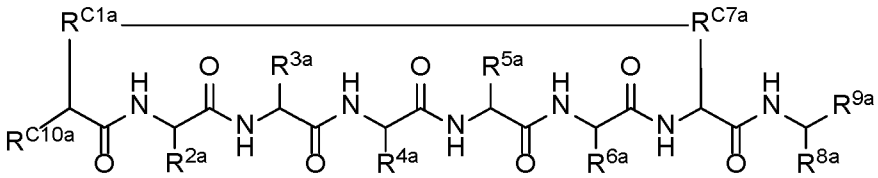
1. A compound of Formula A, Formula B, or Formula C, or a salt or solvate thereof:



[Formula A];



[Formula B]; or



[Formula C];

wherein:

R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is C_1-C_5 alkyl or $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –$N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is –$N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{5a} is -$(CH_2)_{1-3}$-R^{5b}, wherein 1 carbon in -$(CH_2)_{2-3}$- is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

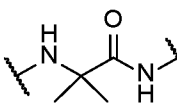
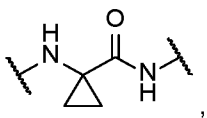
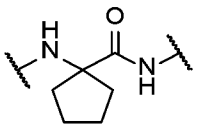
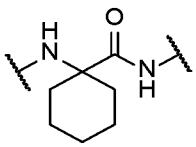
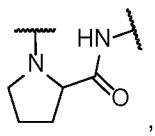
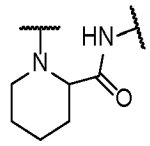
phenyl optionally substituted with one or a combination of the following: 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, -SR^{5c}, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{5c}, -SH, –SR^{5c}, -N_3, or -CN, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$;

wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

either R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -C≡C-$(CH_2)_{1-3}$-OH, -C≡C-$(CH_2)_{1-3}$-SH, -C≡C-$(CH_2)_{1-3}$-NH_2, -C≡C-$(CH_2)_{1-3}$-COOH, -C≡C-$(CH_2)_{1-3}$-$CONH_2$, -C≡C-$(CH_2)_{1-3}$-$R^{6b}R^{6c}$, -CH=CH-$(CH_2)_{1-3}$-OH, -CH=CH-$(CH_2)_{1-3}$-SH, -CH=CH-$(CH_2)_{1-3}$-NH_2, -CH=CH-$(CH_2)_{1-3}$-COOH, -CH=CH-$(CH_2)_{1-3}$-$CONH_2$, -CH=CH-$(CH_2)_{1-3}$-$R^{6b}R^{6c}$, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-, and wherein R^{6c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

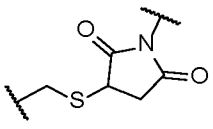
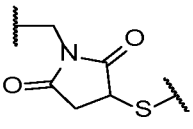
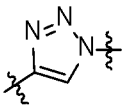
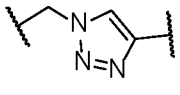
or -NH-CH(R^{6a})-C(O)-NH- is replaced with:


,

,

,

,

,
or

;

R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is -$C(O)NH_2$, -C(O)-OH, -CH_2-$C(O)NH_2$, -CH_2-C(O)-OH, -CH_2-NH_2, -CH_2-OH, -CH_2-CH_2-NH_2, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^{X}_{n1}, wherein:

R^{9b} is -CH_2-NH-C(O)-, -CH_2-C(O)-, -CH_2-O-, -C(O)NH-, -C(O)-N(CH_3)-, -CH_2-NHC(S)-, -C(S)NH-, -CH_2-N(CH_3)C(S)-, -C(O)N(CH_3)-, -CH_2-N(CH_3)C(O)-, -C(S)N(CH_3)-, -CH_2-NHC(S)NH-, -CH_2-NHC(O)NH-, -CH_2-S-, -CH_2-S(O)-, -CH_2-S(O)$_2$-, -CH_2-S(O)$_2$-NH-, -CH_2-S(O)-NH-, -CH_2-Se-, -CH_2-Se(O)-, -CH_2-Se(O)$_2$-, -CH_2-NHNHC(O)-, -C(O)NHNH-, -CH_2-OP(O)(O^-)O-, -CH_2-phosphamide-, -CH_2-thiophosphodiester-, -CH_2-S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

R^{A10} is absent or -[linker]-R^X_{n1};

when R^{A10} is absent, then R^{A1a} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-(CH_3)$_{1-2}$, -NH_2-CH_3, -N(CH_3)$_{2-3}$, -S-CH_3, or -O-CH_3;

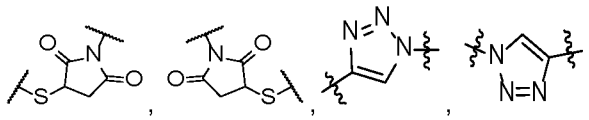
a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

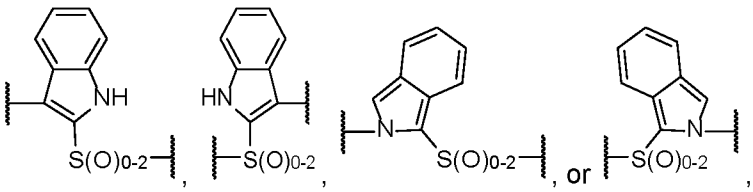
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or N(R^{A1d})$_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

when R^{A10} is -[linker]-R^{X}_{n1}, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-,



, or polyethylene glycol;

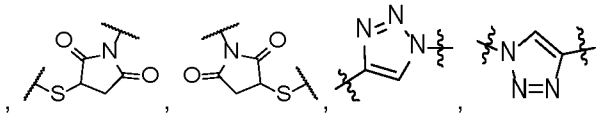
R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, C_2-C_{10} alkenylenyl, or C_2-C_{10} alkynylenyl, wherein one or more carbons in C_2-C_{10} alkylenyl, alkenylenyl, alkynylenyl are optionally independently replaced with N, S, and/or O heteroatoms;

R^{B1-7} is , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NO_2, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

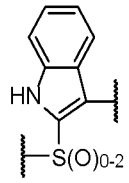
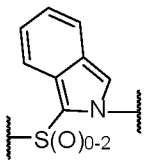
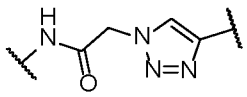
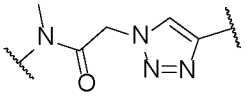
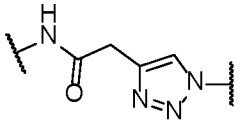
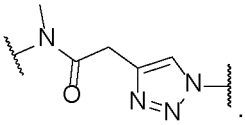
R^{B7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

R^{B10a} is amine, -NH-$(CH_3)_{1-2}$, -$N(CH_3)_{2-3}$, -NH-C(O)-CH_3, -NH-C(O)-(phenyl), or –R^{B10b}-[linker]-R^{X}_{n1} wherein R^{B10b} is:

-NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-



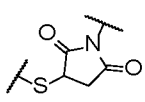
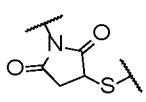
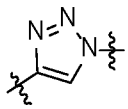
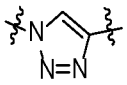
, or polyethylene glycol;

R^{C1a} is , , , , , or ;, wherein the indole, the isoindole, and the triazole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

R^{C7a} is a linear C_1-C_5 alkylenyl, wherein optionally 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

R^{C10a} is R^{C10b}-R^{C10c}-[linker]-R^{X}_{n1} or R^{C10d}, wherein:

R^{C10b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{C10d} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl, wherein 0-3 carbons in C_2-C_{10} alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms; or

$R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

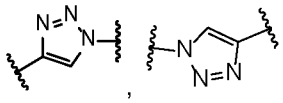
a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, $-OR^{C10g}$, amino, $-NHR^{C10g}$, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is $–N(R^{3g})_{2\text{-}3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

each n1 is independently 0, 1 or 2;

each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled; wherein 0-3 peptide backbone amides are independently replaced with



, amidine, or thioamide;

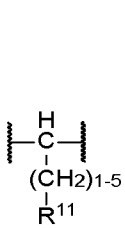
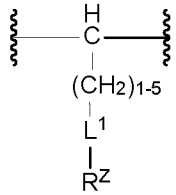
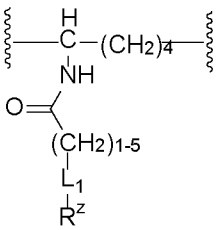
wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

2. The compound of claim 1, wherein:

R^{A10} is -[linker]-$R^X{}_{n1}$;

the linker is X^1L^1, $X^1L^1X^1L^1$, $X^1L^1X^1L^1X^1L^1$;

X^1 is each independently $-CH_2-$, , , or ;

L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, $–N(CH_3)C(O)–$, or $–C(O)N(CH_3)–$;

R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

R^Z is each independently an albumin binder.

3. The compound of claim 1 or 2, wherein:

a) R^{9a} is R^{9b}-[linker] R^{x}_{n1};

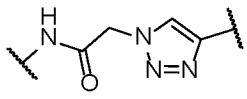
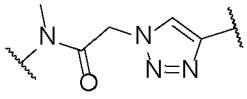
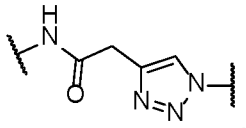
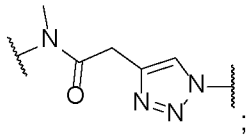
b) R^{3a} is C_1-C_5 alkyl;

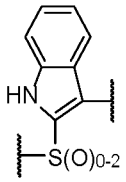
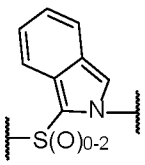
c) R^{y} is $R^{3e}R^{3f}$;

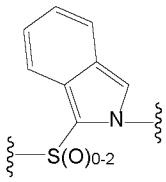
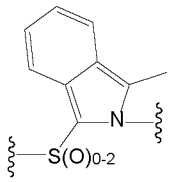
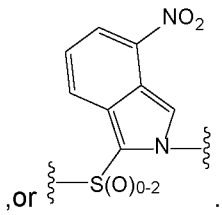
d) at least one peptide backbone amide is N-methylated; or

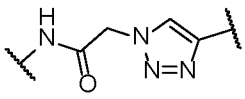
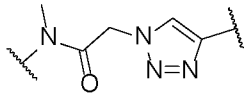
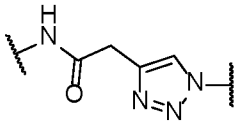
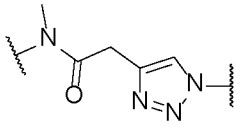
e) at least one peptide backbone amide is replaced with an amidine.

4. The compound of any one of claims 1-3, wherein:

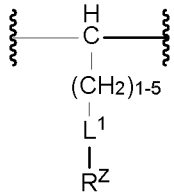
a) R^{C1a} is , , , or ; or

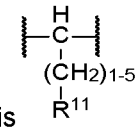
b) R^{C1a} is , or , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NO_2, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl; provided that the compound of Formula C is not cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Cys]-Lys(iPr)-NH_2, cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-Cys]-Lys(iPr)-NH_2, cyclo(isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(Me-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Cys]-Lys(iPr)-NH_2, and cyclo(NO_2-isoindole N^a-S)[Lys(Cys(Acid)-DOTA-Ga)-Tyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-hCys]-Lys(iPr)-NH_2.

5. The compound of any one of claims 1-4, wherein R^{C1a} is , , , or .

6. The compound of claim 1, wherein R^{C1a} is , , , or .

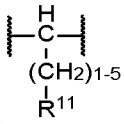
7. The compound of claim 5 or 6, wherein R^{C7a} is linear C_1-C_2 alkylenyl.

8. The compound of claim 2, wherein at least one X^1 is .

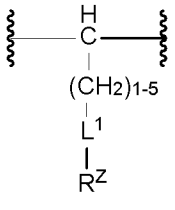
9. The compound of claim 2 or 8, wherein the linker is X^1L^1; X^1 is  ; and L^1 is –NH– or –NHC(O)–.

10. The compound of claim 2 or 8, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

X^{1a} is  ;

L^{1a} is –NH– or –NHC(O)–;

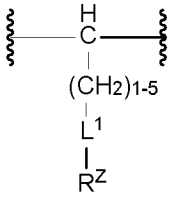


X^{1b} is ; and

L^{1b} is –NH– or –NHC(O)–.

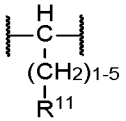
11. The compound of claim 2 or 8, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;



X^{1a} is ;

L^{1a} is –NH– or –NHC(O)–;

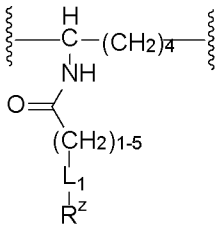


X^{1b} is ; and

L^{1b} is –NH– or –NHC(O)–.

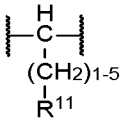
12. The compound of claim 2, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;



X^{1a} is ;

L^{1a} is –NH– or –NHC(O)–;

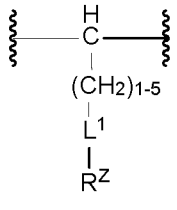


X^{1b} is ; and

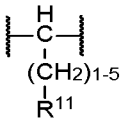
L^{1b} is –NH– or –NHC(O)–.

13. The compound of claim 2 or 8, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;

X^{1a} is  ;

L^{1a} is –NH– or –NHC(O)–;

X^{1b} is  ;

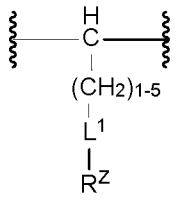
L^{1b} is –NH– or –NHC(O)–;

X^{1c} is $–CH_2–$; and

L^{1c} is –NH— or –NHC(O)–.

14. The compound of claim 2 or 8, wherein:

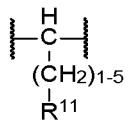
the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;

X^{1a} is  ;

L^{1a} is –NH– or –NHC(O)–;

X^{1b} is $–CH_2–$;

L^{1b} is –NH– or –NHC(O)–;

X^{1c} is  ; and

L^{1c} is –NH– or –NHC(O)–.

15. The compound of any one of claims 2 and 8-14, wherein R^{11} is sulfonic acid ($-SO_3H$).

16. The compound of any one of claims 1-15, wherein:

R^{9a} is R^{9b}-[linker]-R^{x}_{n1}.

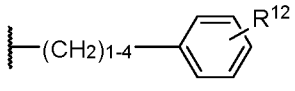
R^{9b} is -C(O)NH-;

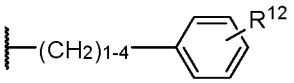
the linker is X^1L^1;

X^1 is $-(CH_2)_{1-5}-$, $-CH(COOH)-(CH_2)_{0-4}-$, or $-CH(CONH_2)-(CH_2)_{0-4}-$; and

L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, $–N(CH_3)C(O)–$, or $–C(O)N(CH_3)–$.

17. The compound of claim 16, wherein R^{x}_{n1} is an albumin binder.

18. The compound of any one of claims 1-17, wherein the albumin binder is $-(CH_2)_{8-20}-CH_3$, $-(CH_2)_{8-20}-C(O)OH$, or , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3.

19. The compound of claim 18, wherein the albumin binder is , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3.

20. The compound of any one of claims 1-19, wherein at least one peptide backbone amide is N-methylated.

21. The compound of any one of claims 1-20, wherein R^{y} is methyl.

22. The compound of any one of claims 1-21, wherein at least one peptide backbone amide is replaced with an amidine.

23. The compound of any one of claims 1-22, wherein the amide backbone between R^{3a} and R^{4a}; between R^{4a} and R^{5a}; or between R^{5a} and R^{6a} is replaced with amidine (-CH(R^{3a})-C(=N)-NH-CH(R^{4a})-, -CH(R^{4a})-C(=N)-NH-CH(R^{5a})- or -CH(R^{5a})-C(=N)-NH-CH(R^{6a})-).

24. The compound of any one of claims 1-23, wherein R^{y} is $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is $–N(R^{3g})_2$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl.

25. The compound of claim 24, wherein R^{3a} is methyl.

26. The compound of claim 1, wherein R^{2a} is $-(CH_2)-(R^{2b})-$(phenyl), wherein R^{2b} is absent, $-CH_2-$, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, $-N_3$, -CN, or -O-phenyl, or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group.

27. The compound of any of claims 1-26, wherein -NH-CH(R^{2a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue.

28. The compound of any one of claims 1-27, wherein -NH-CH(R^{2a})-C(O)- of Formula A, Formula B, or Formula C forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue.

29. The compound of any one of claims 1-22 and 26-28, wherein R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{3c} is –$N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl.

30. The compound of any one of claims 1-29, wherein -NR^y-CH(R^{3a})-C(O)- of Formula A or -NH-CH(R^{3a})-C(O)- of Formula B or Formula C forms an L-amino acid residue.

31. The compound of any one of claims 1-29, wherein -NR^y-CH(R^{3a})-C(O)- of Formula A or -NH-CH(R^{3a})-C(O)- of Formula B, or Formula C forms a Lys(iPr) residue, a $Arg(Me)_2$ (asymmetrical) residue, or a Arg(Me) residue.

32. The compound of any one of claims 1-31, wherein R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is –$N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl.

33. The compound of any one of claims 1-32, wherein -NH-CH(R^{4a})-C(O)- of Formula A, Formula B, or Formula C forms a D-amino acid residue.

34. The compound of any one of claims 1-33, wherein -NH-CH(R^{4a})-C(O)- forms a D-Arg residue or a D-hArg residue.

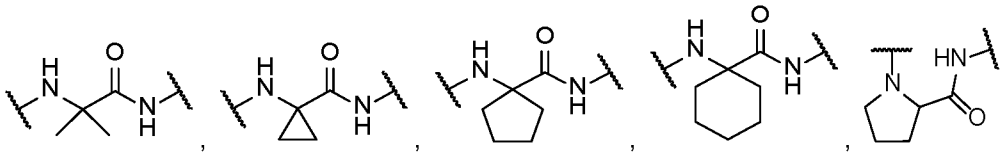
35. The compound of any one of claims 1-34, wherein R^{5a} is -$(CH_2)_{1-3}$-R^{5b}, wherein R^{5b} is:
phenyl optionally substituted with one or a more of the following: 4-substituted with -NH_2, -NO_2, -OH, -SH, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH; or
a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$; and
wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group.

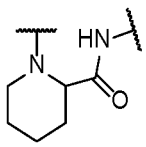
36. The compound of any one of claims 1-35, wherein -NH-CH(R^{5a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue.

37. The compound of any one of claims 1-36, wherein -NH-CH(R^{5a})-C(O)- of Formula A, Formula B, or Formula C forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue.

38. The compound of any one of claims 1-37, wherein R^{6a} is H, methyl, ethyl, -C≡CH, -$CH=CH_2$, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen.

39. The compound of any one of claims 1-37, wherein -NH-CH(R^{6a})-C(O)-NH- of Formula A, Formula B, or Formula C is replaced with:


, or


.

40. The compound of any one of claims 1-39, wherein -NH-CH(R^{6a})-C(O)- of Formula A, Formula B, or Formula C forms a D-amino acid residue.

41. The compound of any one of claims 1-40, wherein -NH-CH(R^{6a})-C(O)- of Formula A, Formula B, or Formula C forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue.

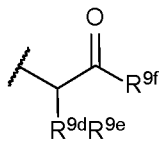
42. The compound of any one of claims 1-41, wherein R^{8a} is $R^{8b}R^{8c}$, wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl.

43. The compound of any one of claims 1-42, wherein:

R^{9a} is -C(O)NH_2, -C(O)-OH, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^{X}_{n1}; and
R^{9b} is -C(O)NH-, -C(O)-N(CH_3)-, -C(O)N(CH_3)-, or -C(O)NHNH-.

44. The compound of any one of claims 1-43, wherein -NH-CH(R^{8a})- together with -C(O)- from R^{9a} in Formula A, Formula B, or Formula C forms an L-amino acid residue.

45. The compound of any one of claims 1-44, wherein -NH-CH(R^{8a})- together with -C(O)- from R^{9a} in Formula A, Formula B, or Formula C forms a Lys(iPr) residue.

46. The compound of any one of claims 1-45, wherein R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-R^{9c}; R^{9b} is –C(O)NH–; and R^{9c} is 

, wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-CH_3, -N(CH_3)$_2$, -S-CH_3, -O-CH_3, or phenyl, and R^{9f} is amino or –OH.

47. The compound of any one of claims 1-45, wherein R^{9a} is -R^{9b}-[linker]-R^{X}_{n1}.

48. The compound of any one of claims 1-47, wherein R^{9b} is –C(O)NH–.

49. The compound of any one of claims 1-48, wherein -NH-CH(R^{A1a})-C(O)- of Formula A forms an L-amino acid residue.

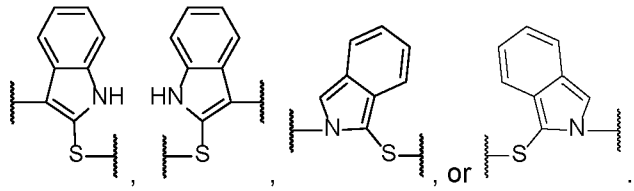
50. The compound of any one of claims 1-49, wherein -NH-CH(R^{A1a})-C(O)- of Formula A, forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue.

51. The compound of any one of claims 1-50, wherein R^{A10} is -[linker]-R^{X}_{n1}.

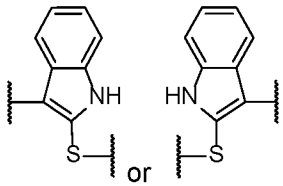
52. The compound of any one of claims 1-51, wherein -NH-CH(R^{A7a})-C(O)- of Formula A forms a D-amino acid residue.

53. The compound of any one of claims 1-52, wherein R^{A7a} is C_1-C_3 alkyl.

54. The compound of any one of claims 1-53, wherein R^{B1-7} is

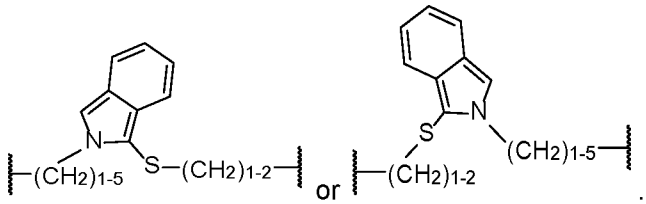


55. The compound of any one of claims 1-48, wherein R^{B1a} is $-(CH_2)_{1-2}$-, R^{B1-7} is



, and R^{B7a} is $-(CH_2)_{1-2}$-.

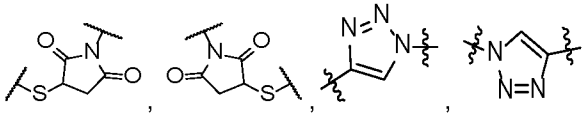
56. The compound of any one of claims 1-47, wherein R^{B1a}-R^{B1-7}-R^{B7a} is



57. The compound of any one of claims 1-48 and 54-56, wherein -NH-CH(R^{B7a})-C(O)- of Formula B forms a D-amino acid residue.

58. The compound of any one of claims 1-48 and 54-57, wherein R^{B10a} is: amine, -NH-$(CH_3)_{1-2}$, -N$(CH_3)_{2-3}$, -NH-C(O)-CH_3, or -NH-C(O)-(phenyl).

59. The compound of any one of claims 1-48 and 54-58, wherein R^{B10a} is -R^{B10b}-[linker]-R^{X}_{n1}.

60. The compound of claim 59, wherein R^{B10b} is:
-NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -NHNHC(O)-, -C(O)NHNH-, , or polyethylene glycol.

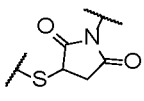
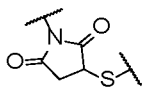
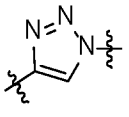
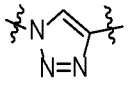
61. The compound of claim 59, wherein R^{B10a} is –NHC(O)-[linker]-R^{X}_{n1} or –N(CH_3)C(O)-[linker]-R^{X}_{n1}.

62. The compound of any one of claims 1-48, wherein -NH-CH(R^{C7a})-C(O)- of Formula C forms a D-amino acid residue.

63. The compound of any one of claims 1-48 and 62, wherein R^{C7a} is a linear C_1-C_5 alkylenyl.

64. The compound of any one of claims 1-48 and 62-63, wherein R^{C10a} is R^{C10b}-R^{C10c}-[linker]-R^{X}_{n1}.

65. The compound of claim 64, wherein R^{C10b} is a linear C_1-C_5 alkylenyl; and R^{C10c} is:

-NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol.

66. The compound of any one of claims 1-48 and 61-63, wherein R^{C10a} is R^{C10d}, wherein R^{C10d} is:

a) a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -N$(CH_3)_{2\text{-}3}$, -S-CH_3, -O-CH_3;

b) a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl; or

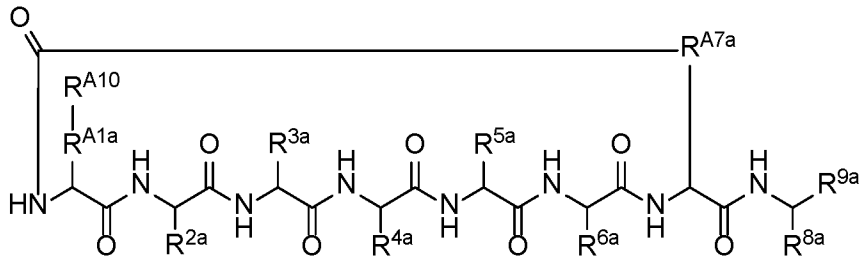
c) $R^{C10e}R^{C10f}$;

wherein R^{C10e} is a linear C_1-C_3 alkyl; and R^{C10f} is

(i) a 5 or 6 membered aromatic ring wherein 0-4 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-4 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

(ii) a fused bicyclic or fused tricyclic aryl group wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-6 groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or N$(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl.

67. The compound of claim 1, wherein the compound has the structure of Formula A-I or salt or solvate thereof:



[Formula A-I];

wherein:

R^{2a} is $-(CH_2)-(R^{2b})-$(phenyl), wherein R^{2b} is absent, $-CH_2-$, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, $-N_3$, -CN, or -O-phenyl or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{3c} is $–N(R^{3d})_{2\text{-}3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is $–N(R^{4d})_{2\text{-}3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{5a} is $-(CH_2)_{1\text{-}3}-R^{5b}$, wherein R^{5b} is:

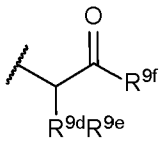
phenyl optionally substituted with one or a more of the following: 4-substituted with $-NH_2$, $-NO_2$, -OH, -SH, $-N_3$, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH;

a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$; and wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-CH_2-R^{6b}$-OH, $-CH_2-R^{6b}$-COOH, $-CH_2-(R^{6b})_{1\text{-}3}-NH_2$, $-CH_2-R^{6b}-CONH_2$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is $–N(R^{8d})_{2\text{-}3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, -R^{9b}-R^{9c} or -R^{9b}-[linker]-R^{X}_{n1};



wherein R^{9b} is –C(O)NH–; and R^{9c} is , wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-CH_3, -N(CH_3)$_2$, -S-CH_3, -O-CH_3, or phenyl, and R^{9f} is amino or –OH;

R^{A7a} is C_1-C_3 alkylenyl;

R^{A10} is absent or -[linker]-R^{X}_{n1};

when R^{A10} is absent, then R^{A1a} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-(CH_3)$_{1-2}$, -NH_2-CH_3, -N(CH_3)$_{2-3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

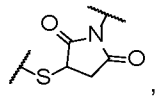
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or N(R^{A1d})$_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

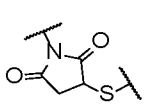
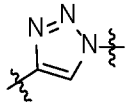
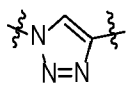
when R^{A10} is -[linker]-R^{X}_{n1}, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

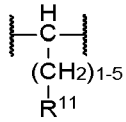
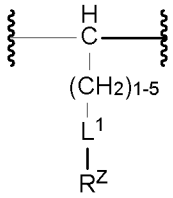
R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -

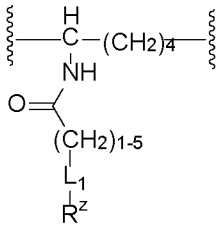
NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -$OP(O)(O^-)O$-, -

phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, ,

, , , or polyethylene glycol;

the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

X^1 is each independently -CH_2-, ,  or

;

L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, or –C(O)$N(CH_3)$–;

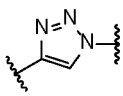
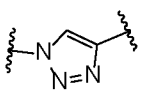
R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

R^Z is each independently an albumin binder;

each n1 is independently 0, 1 or 2;

each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

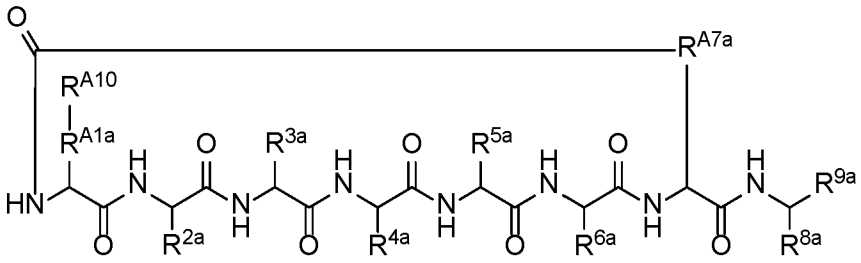
wherein 0-3 peptide backbone amides are independently replaced with

, , amidine, or thioamide;

wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

68. The compound of claim 1 or 67, wherein the compound has the structure of Formula A-II or salt or solvate thereof:



[Formula A-II];

wherein:

-NH-CH(R^{2a})-C(O)- in Formula A-II forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

-NH-CH(R^{3a})-C(O)- in Formula A-II forms a Lys(iPr) residue, a Arg(Me)$_2$ (asymmetrical) residue, or a Arg(Me) residue;

-NH-CH(R^{4a})-C(O)- in Formula A-II forms a D-Arg residue or a D-hArg residue;

-NH-CH(R^{5a})-C(O)- in Formula A-II forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

-NH-CH(R^{6a})-C(O)- in Formula A-II forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –N(R^{8d})$_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-[linker]-R^X_{n1};

R^{9b} is –C(O)NH–;

R^{A7a} is C_1-C_3 alkylenyl;

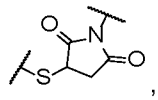
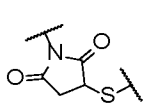
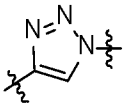
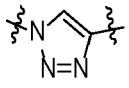
R^{A10} is absent or -[linker]-R^X_{n1};

when R^{A10} is absent, then R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-(CH_3)$_{1-2}$, -NH_2-CH_3, -N(CH_3)$_{2-3}$, -S-CH_3, -O-CH_3, or a branched C_1-C_{10} alkyl, alkenyl, or alkynyl;

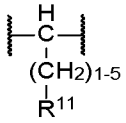
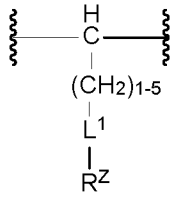
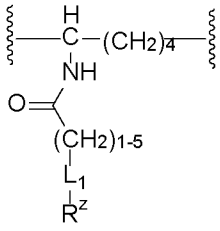
when R^{A10} is -[linker]-R^X_{n1}, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S(O)$_2$-, -S(O)$_2$-O-, -S(O)$_2$-NH-, -S(O)-NH-,

-Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -$OP(O)(O^-)O$-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

X^1 is each independently -CH_2-, , , or ;

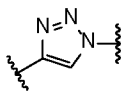
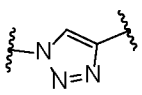
L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –$N(CH_3)C(O)$–, or –$C(O)N(CH_3)$–;

R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

R^Z is each independently an albumin binder;

each n1 is independently 0, 1 or 2;

each R^X is an albumin binder, a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

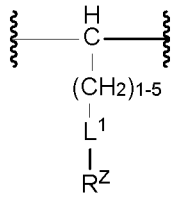
wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

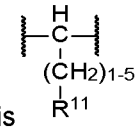
wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

69. The compound of claim 67 or 68, wherein -NH-CH(R^{A1a})-C(O)- of Formula A-I or Formula A-II forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, a Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue.

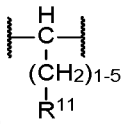
70. The compound of any one of claims 67-69, wherein R^{A10} is -[linker]-R^{X}_{n1} and R^{9a} is -$C(O)NH_2$, -C(O)-OH, -CH_2-$C(O)NH_2$, or -CH_2-C(O)-OH.

71. The compound of any one of claims 67-70, wherein at least one X^1 is .

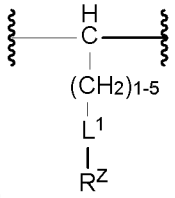
72. The compound of any one of claims 67-70, wherein the linker is X^1L^1; X^1 is  ; and L^1 is –NH– or –NHC(O)–.

73. The compound of any one of claims 67-70, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

X^{1a} is  ;

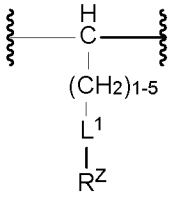
L^{1a} is –NH– or –NHC(O)–;

X^{1b} is  ; and

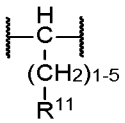
L^{1b} is –NH– or –NHC(O)–.

74. The compound of any one of claims 67-70, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;

X^{1a} is  ;

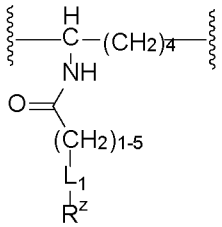
L^{1a} is –NH– or –NHC(O)–;

X^{1b} is  ; and

L^{1b} is –NH– or –NHC(O)–.

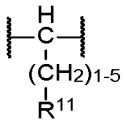
75. The compound of any one of claims 67-70, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}$;



X^{1a} is ;

L^{1a} is –NH– or –NHC(O)–;

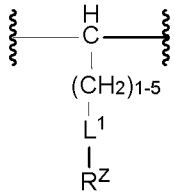


X^{1b} is ; and

L^{1b} is –NH– or –NHC(O)–;.

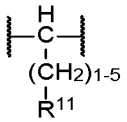
76. The compound of any one of claims 67-70, wherein:

the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;



X^{1a} is ;

L^{1a} is –NH– or –NHC(O)–;



X^{1b} is ;

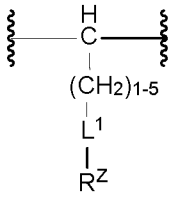
L^{1b} is –NH– or –NHC(O)–;

X^{1c} is $–CH_2–$; and

L^{1c} is –NH– or –NHC(O)–;.

77. The compound of any one of claims 67-70, wherein:

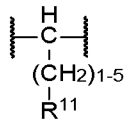
the linker is $X^{1a}L^{1a}X^{1b}L^{1b}X^{1c}L^{1c}$;

X^{1a} is  ;

L^{1a} is –NH– or –NHC(O)–;

X^{1b} is $–CH_2–$;

L^{1b} is –NH– or –NHC(O)–;

X^{1c} is  ; and

L^{1c} is –NH– or –NHC(O)–;.

78. The compound of any one of claims 67-77, wherein R^{11} is sulfonic acid ($-SO_3H$).

79. The compound of any one of claims 67-78, wherein:

R^{9a} is R^{9b}-[linker]-R^x_{n1}.

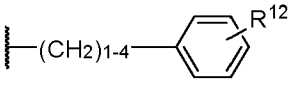
R^{9b} is -C(O)NH-;

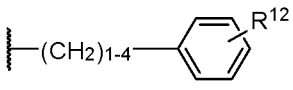
the linker is X^1L^1;

X^1 is $-(CH_2)_{1-5}$-, $-CH(COOH)-(CH_2)_{0-4}$-, or $-CH(CONH_2)-(CH_2)_{0-4}$-; and

L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, $–N(CH_3)C(O)–$, or $–C(O)N(CH_3)–$.

80. The compound of claim 79, wherein R^x is an albumin binder.

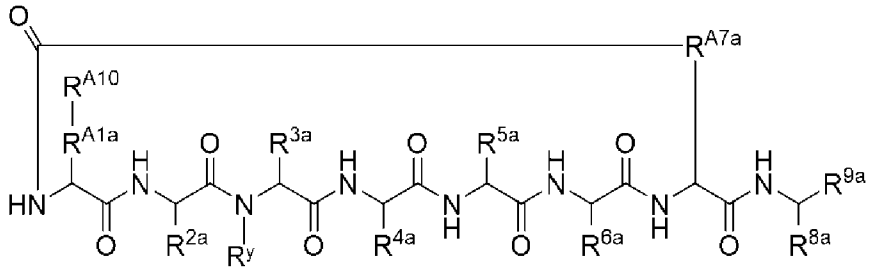
81. The compound of any one of claims 67-80, wherein the albumin binder is $-(CH_2)_{8-20}-CH_3$, $-(CH_2)_{8-20}-C(O)OH$, or  , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3.

82. The compound of claim 81, wherein the albumin binder is  , wherein R^{12} is I, Br, F, Cl, H, OH, OCH_3, NH_2, NO_2 or CH_3.

83. The compound of any one of claims 67-82, wherein one peptide backbone amide is N-methylated.

84. The compound of any one of claims 67-83, wherein one peptide backbone carbonyl is replaced with an imino.

85. The compound of claim 1, wherein the compound has the structure of Formula A-III or salt or solvate thereof:



[Formula A-III];

wherein:

R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, -N_3, -CN, or -O-phenyl or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is C_1-C_5 alkyl;

R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2\text{-}3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is –$N(R^{4d})_{2\text{-}3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{5a} is -$(CH_2)_{1\text{-}3}$-R^{5b}, wherein R^{5b} is:

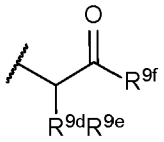
phenyl optionally substituted with one or a more of the following: 4-substituted with -NH_2, -NO_2, -OH, -SH, -N_3, -CN, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH;

a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$; and wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1\text{-}3}$-NH_2, -CH_2-R^{6b}-$CONH_2$, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is $-C(O)NH_2$, $-C(O)-OH$, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, $-R^{9b}-R^{9c}$ or $-R^{9b}$-[linker]-$R^X{}_{n1}$;

wherein R^{9b} is –C(O)NH–; and R^{9c} is , wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-CH_3$, $-N(CH_3)_2$, $-S-CH_3$, $-O-CH_3$, or phenyl, and R^{9f} is amino or –OH;

R^{A7a} is C_1-C_3 alkylenyl;

R^{A10} is absent or -[linker]-$R^X{}_{n1}$;

when R^{A10} is absent, then R^{A1a} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-(CH_3)_{1-2}$, $-NH_2-CH_3$, $-N(CH_3)_{2-3}$, $-S-CH_3$, or $-O-CH_3$;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

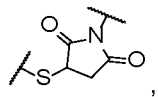
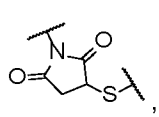
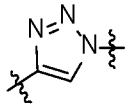
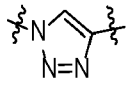
$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

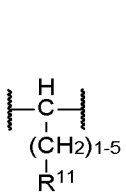
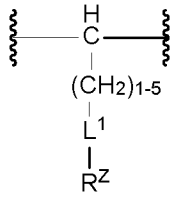
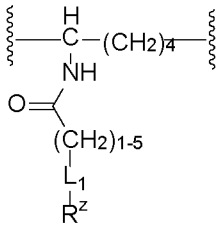
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, $-OR^{A1d}$, amino, $-NHR^{A1d}$, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$;

X^1 is each independently -CH_2-, , , ;

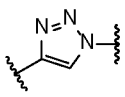
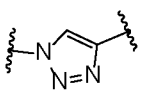
L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, or –C(O)N(CH_3)–;

R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

R^Z is each independently an albumin binder;

each n1 is independently 0, 1 or 2;

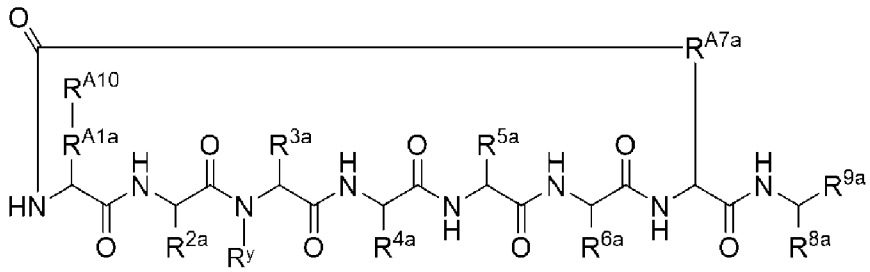
each R^X is an albumin binder, therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

86. The compound of claim 1 or 85, wherein the compound has the structure of Formula A-IV or salt or solvate thereof:



[Formula A-IV];

wherein:

-NH-CH(R^{2a})-C(O)- in Formula A-IV forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

-NH-CH(R^{4a})-C(O)- in Formula A-IV forms a D-Arg residue or a D-hArg residue;

-NH-CH(R^{5a})-C(O)- in Formula A-IV forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

-NH-CH(R^{6a})-C(O)- in Formula A-IV forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

R^{3a} is C_1-C_5 alkyl;

R^y is hydrogen or $R^{3e}R^{3f}$ wherein R^{3e} is a linear C_1-C_5 alkylenyl, wherein R^{3f} is –$N(R^{3g})_{2-3}$, wherein each R^{3g} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-[linker]-$R^X{}_{n1}$;

R^{9b} is –C(O)NH–;

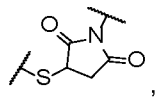
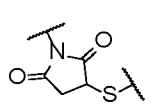
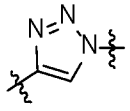
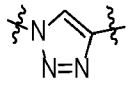
R^{A7a} is C_1-C_3 alkylenyl;

R^{A10} is absent or -[linker]-$R^X{}_{n1}$;

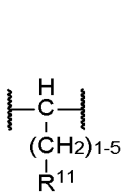
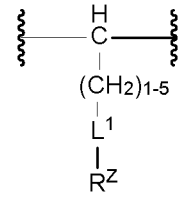
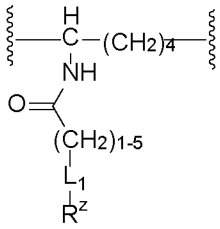
when R^{A10} is absent, then R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, -O-CH_3, or a branched C_1-C_{10} alkyl, alkenyl, or alkynyl;

when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein:

R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1LX^1L^1X^1L^1$;

X^1 is each independently -CH_2-, , , or ;

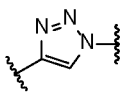
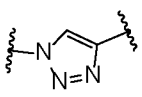
L^1 is each independently –NH–, –C(O)–, –NHC(O)–, –C(O)NH–, –N(CH_3)C(O)–, or –C(O)N(CH_3)–;

R^{11} is each independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; and

R^Z is each independently an albumin binder;

each n1 is independently 0, 1 or 2;

each R^X is an albumin binder, a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

wherein 0-3 peptide backbone amides are independently replaced with , , amidine, or thioamide;

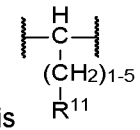
wherein 0-3 peptide backbone amides are N-methylated; and

wherein C-terminal is optionally amidated.

87. The compound of claim 85 or 86, wherein -NH-CH(R^{A1a})-C(O)- of Formula A-III or Formula A-IV forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, a Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue.

88. The compound of any one of claims 85-87, wherein R^y is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, wherein R^{3c} is $–N(R^{3d})_2$, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl.

89. The compound of claim 88, wherein R^{3a} is methyl.

90. The compound of any one of claims 85-89, wherein the linker is X^1L^1; X^1 is  ; and L^1 is –NH– or –NHC(O)–.

91. The compound of any one of claims 85-90, wherein R^{11} is sulfonic acid (-SO_3H).

92. The compound of any one of claims 1-89, wherein:
R^{9a} is -C(O)NH_2, -C(O)-OH, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-$R^X{}_{n1}$; and
R^{9b} is -C(O)NH-.

93. The compound of any one of claims 1-92, wherein zero peptide backbone amides are replaced.

94. The compound of any one of claims 1-93, wherein one peptide backbone amide is N-methylated.

95. The compound of any one of claims 1-19, 21-82, and 84-93, wherein zero peptide backbone amides are N-methylated.

96. The compound of any one of claims 1-95, wherein the compound of Formula A, Formula A-I, or Formula A-II, Formula A-III, Formula A-IV, or a salt or solvate thereof have the following combinations:

(1) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(2) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NCH_3-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(3) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(=NH)-, wherein R^{5a} is a -CH_2(2-naphthyl);
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(4) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(=NH)-, wherein R^{4a} is –$(CH_2)_3NHC(=NH)NH_2$;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(5) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(=NH)-, wherein R^{3a} is –$(CH_2)_4NH(iPr)$;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue; or

(6) -NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue; and
wherein R^y is -$(CH_2)_4$-NH-(iPr) and R^{3a} is -CH_3.

97. The compound of any of claims 1 to 66 and 93 to 95, wherein the compound of Formula B, or a salt or solvate thereof have the following combinations:
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and
-NH-CH(R^{6a})-C(O)- forms a D-Ala.

98. The compound of any of claims 1 to 66 and 93 to 95, wherein the compound of Formula C, or a salt or solvate thereof have the following combinations:
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue; and
-NH-CH(R^{6a})-C(O)- forms a D-Ala.

99. The compound of any one of claims 1 to 98, wherein at least one R^X is a radiolabeled group or a group capable of being radiolabelled.

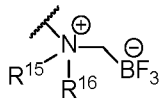
100. The compound of any one of claims 1 to 99, wherein each group capable of being radiolabelled is independently selected from: a metal chelator optionally in complex with a radiometal or radioisotope-bound metal; a prosthetic group containing trifluoroborate (BF_3); or a prosthetic group containing a silicon-fluorine-acceptor moiety, a sulphonyl fluoride, or a phosphoryl fluoride.

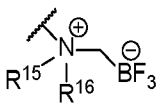
101. The compound of claim 100, wherein the metal chelator is in complex with the radioisotope.

102. The compound of claim 100 or 101, wherein the metal chelator is a polyaminocarboxylate chelator.

103. The compound of claim 100 or 101, wherein the metal chelator is DOTA, MACROPA, or a derivative thereof.

104. The compound of claim 100 or 101, wherein the metal chelator is selected from Table 3.

105. The compound of claim 100, wherein the prosthetic group containing BF_3 is $–R^{13}R^{14}BF_3$ wherein R^{13} is $–(CH_2)_{1\text{-}5}–$ and $–R^{14}BF_3$ is selected from Table 5 or Table 6 or is ; wherein each R^{15} and each R^{16} are independently a branched or linear C_1-C_5 alkyl.

106. The compound of claim 105, wherein $–R^{14}BF_3$ is .

107. The compound of claim 106, wherein R^{15} and R^{16} are each methyl.

108. The compound of any one of claims 100 and 105-107, wherein the prosthetic group containing BF_3 comprises at least one ^{18}F.

109. The compound of any one of claims 1-108, wherein at least one R^X is a therapeutic moiety.

110. The compound of any one of claims 1-109, wherein at least one R^X is fluorescent label.

111. A compound selected from one or more of:

cyclo[Lys-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys(ivDde)-Tyr-NMe-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys(ivDde)-Tyr-(N-isopropylbutan-1-amine)-D-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo(Ttn)[β-Ala(iPr)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2;

cyclo(Ttn)[D-β-Ala(iPr)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-Cys]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys(ivDde)-Tyr-(N-isopropylbutan-1-amine)-Ala-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys(ivDde)-Tyr-Lys(iPr)-D-Arg-2Nal-Ψ-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys(ivDde)-Tyr-Lys(iPr)-D-Arg-Ψ-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

cyclo[Lys-NH_2-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2; or

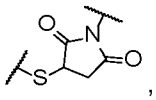
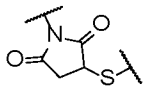
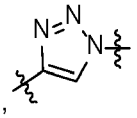
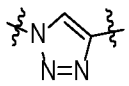
cyclo[Lys(ivDde)-Tyr-Lys(iPr)-Ψ-D-Arg-2Nal-D-Ala-D-Glu]Lys(iPr)-NH_2;

or a salt or solvate thereof;

wherein the compound is optionally bound to a radiolabeled group, a group capable of being radiolabelled, and/or albumin binder, optionally through one or more linkers.

112. The compound of claim 111, wherein the linker is each independently a linear or branched chain of 1-10 units of X^1L^1 and/or $X^1(L^1)_2$, wherein:

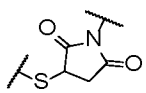
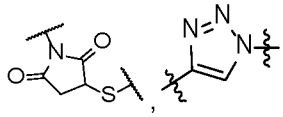
each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid; and

each L^1 is independently -NH-C(O)-, -NH-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; or

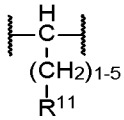
alternatively, the linker is a linear or branched peptide linker $(Xaa)_{1-5}$, wherein each Xaa is independently selected from a proteinogenic amino acid residue or a nonproteinogenic amino acid residue; and wherein an amino group in each Xaa is optionally methylated.

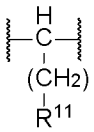
113. The compound of claim 111 or 112, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different and each L^1 is same or different; wherein:

each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid; and

each L^1 is independently -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , or polyethylene glycol.

114. The compound of claim 112 or 113, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different and each L^1 is same or different; and

X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.

115. The compound of claim 112 or 113, wherein each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.

116. The compound of claim 112, wherein the linker is a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in each Xaa is optionally methylated.

117. The compound of claim 112, wherein the linker is a single amino acid residue selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group the single amino acid residue is optionally methylated.

118. The compound of claim 112, wherein the linker is a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from Dap, Dab, Orn, Arg, hArg, Agb, Agp, Acp, Pip, or N^{ε}, N^{ε}, N^{ε}-trimethyl-lysine; and wherein an amino group in each Xaa is optionally methylated.

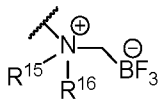
119. The compound of claim 112, wherein the linker is a single amino acid residue selected from D-Arg, L-Arg, D-hArg, L-hArg, or Pip; and wherein an amino group in the single amino acid residue is optionally methylated.

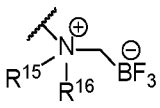
120. The compound of any one of claims 111-119, wherein the group capable of being radiolabelled is independently selected from: a metal chelator optionally in complex with a radiometal or radioisotope-bound metal; a prosthetic group containing trifluoroborate (BF_3); or a prosthetic group containing a silicon-fluorine-acceptor moiety, a sulphonyl fluoride, or a phosphoryl fluoride.

121. The compound of claim 120, wherein the metal chelator is in complex with the radioisotope.

122. The compound of claim 120 or 121, wherein the metal chelator is DOTA, H2-MACROPA, or a derivative thereof.

123. The compound of claim 120 or 121, wherein the metal chelator is selected from Table 3.

124. The compound of claim 120, wherein the prosthetic group containing BF_3 is $–R^{13}R^{14}BF_3$ wherein R^{13} is $–(CH_2)_{1\text{-}5}–$ and $–R^{14}BF_3$ is selected from Table 5 or Table 6 or is ; wherein each R^{15} and each R^{16} are independently a branched or linear C_1-C_5 alkyl.

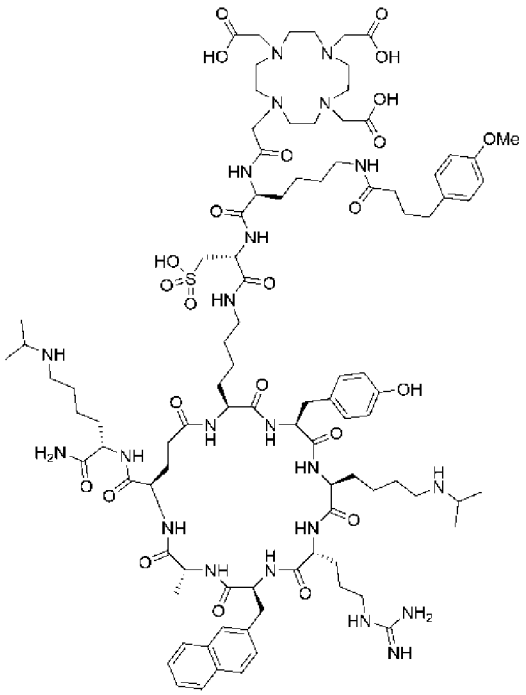
125. The compound of claim 124, wherein $–R^{14}BF_3$ is , wherein R^{15} and R^{16} are each methyl.

126. The compound of any one of claims 120, 124, and 125, wherein the prosthetic group containing BF_3 comprises at least one ^{18}F.

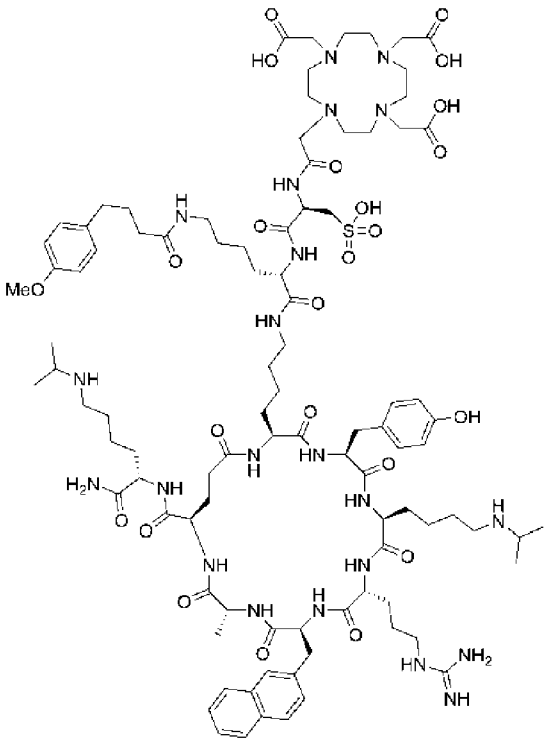
127. The compound of any one of claims 100-104 and 120-123, wherein the radioisotope is ^{64}Cu, ^{67}Cu, ^{90}Y, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{213}Bi, ^{224}Ra, ^{212}Bi, ^{212}Pb, ^{227}Th, ^{223}Ra, ^{47}Sc, ^{186}Re,^{188}Re, ^{94m}Tc, ^{68}Ga, ^{61}Cu, ^{67}Ga, ^{99m}Tc, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{117m}Sn, ^{165}Er, ^{211}At, ^{203}Pb, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{152}Tb, ^{155}Tb, or ^{114m}In.

128. The compound of claim 127, wherein the radioisotope is ^{177}Lu, ^{111}In, ^{213}Bi, ^{68}Ga, ^{67}Ga, ^{203}Pb, ^{212}Pb, ^{44}Sc, ^{47}Sc, ^{90}Y, ^{86}Y, ^{225}Ac, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{165}Er, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{64}Cu, ^{155}Tb, ^{155}Tb, or ^{67}Cu.

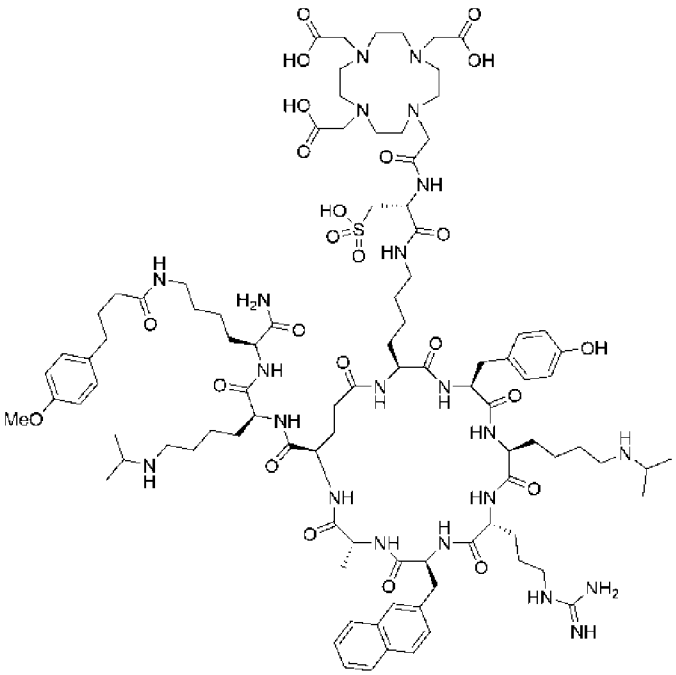
129. The compound of claim 1 of Formula A having the following chemical formula:



;

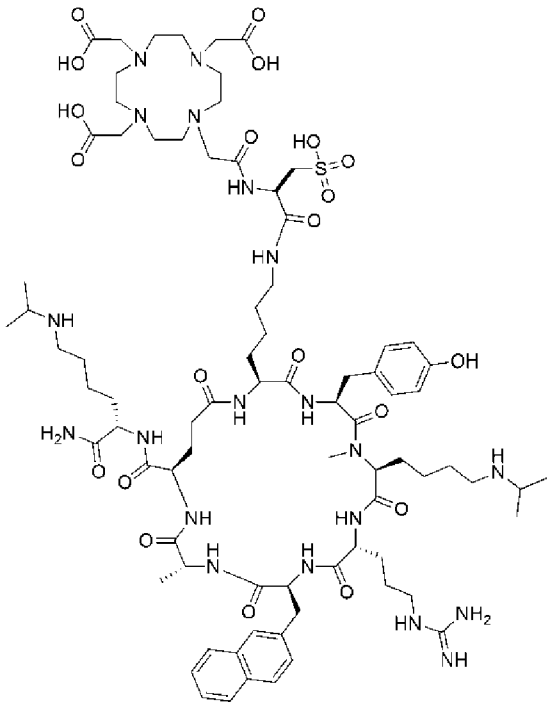


; or



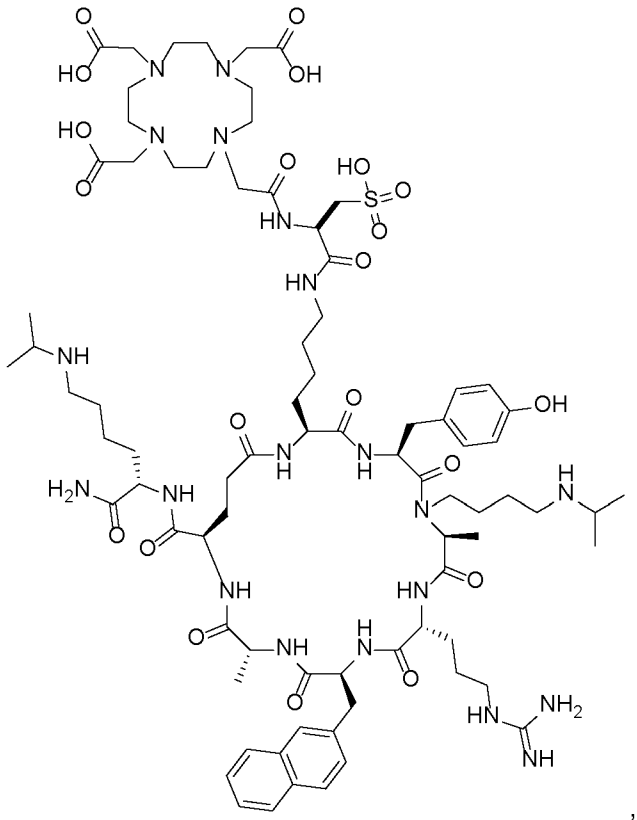
, or salt or solvate thereof.

130. The compound of claim 1 of Formula A having the following chemical formula:



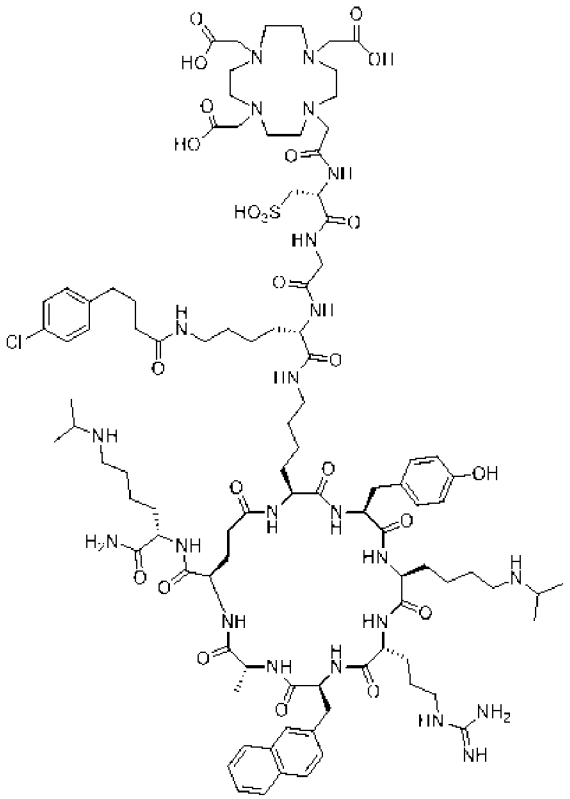
, or salt or solvate thereof.

131. The compound of claim 1 of Formula A having the following chemical formula:

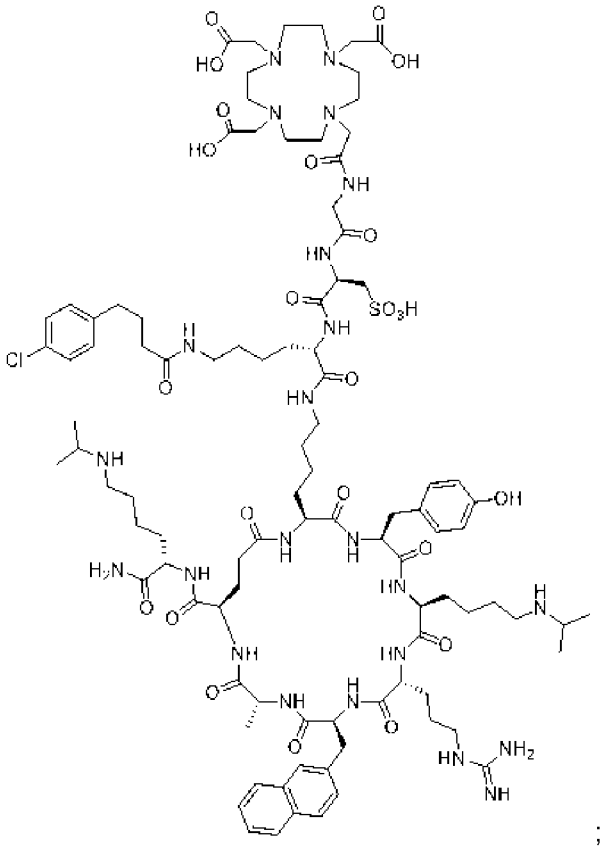


, or salt or solvate thereof.

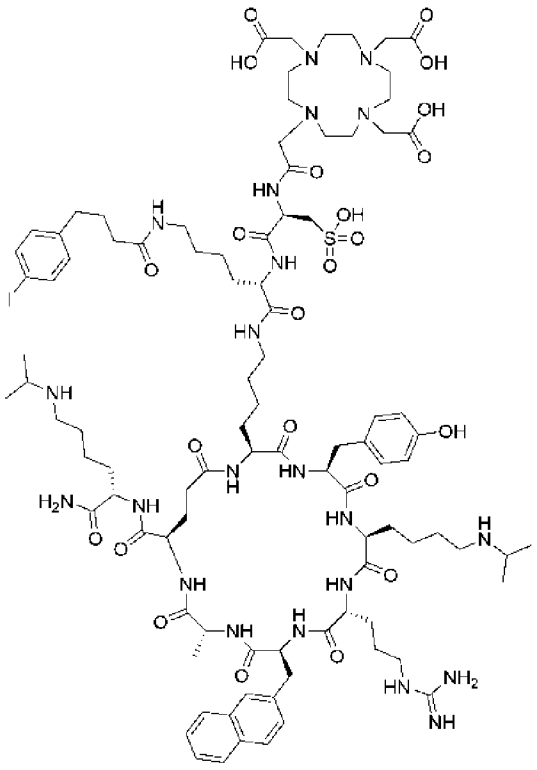
132. The compound of claim 1 of Formula A having the following chemical formula:



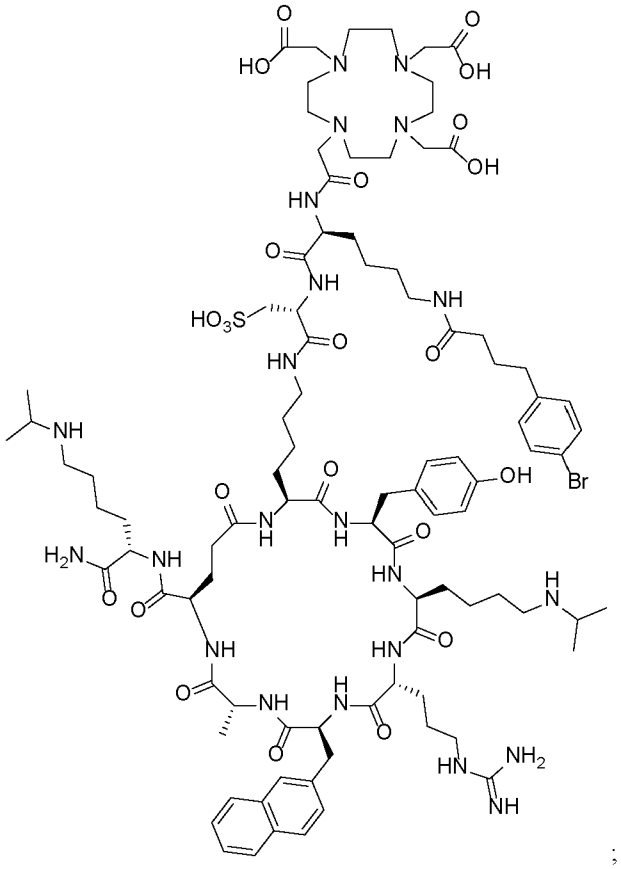
;



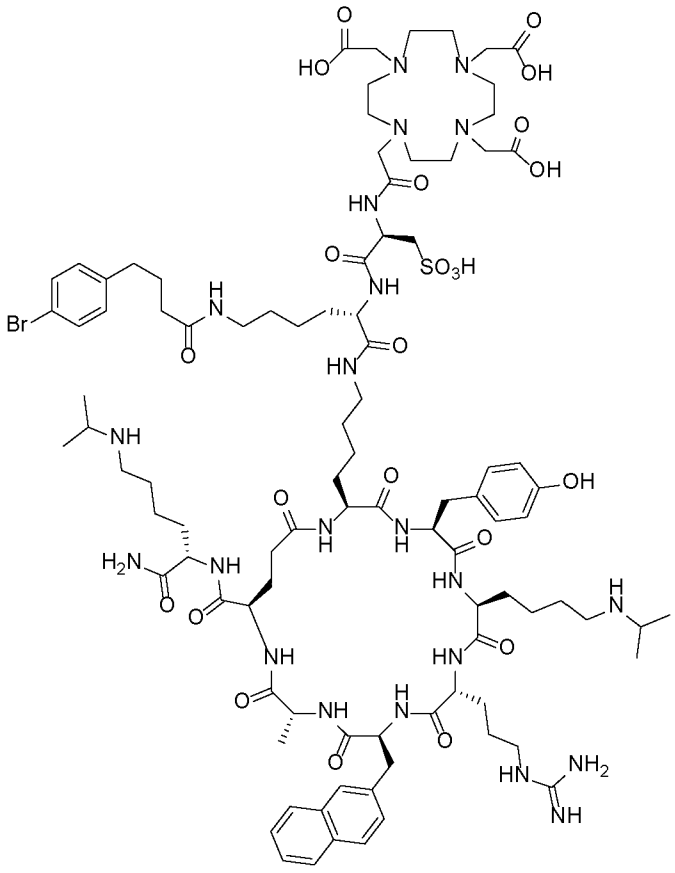
;



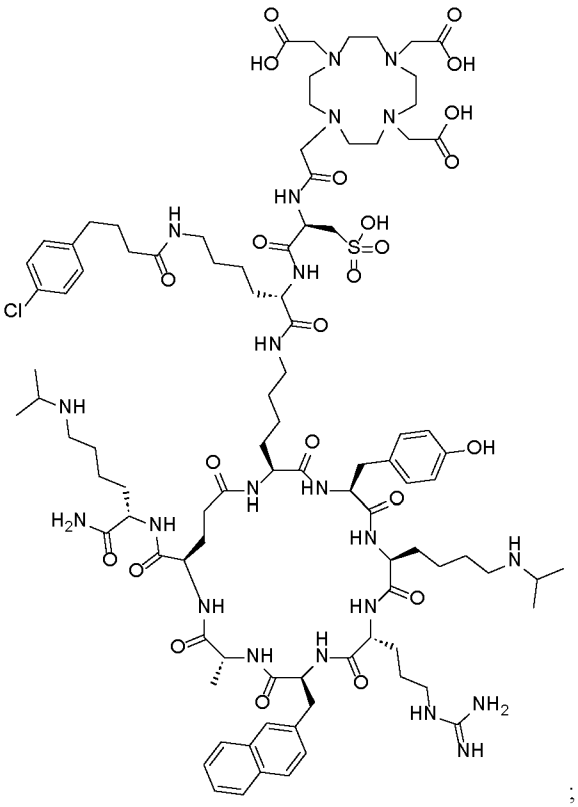
;



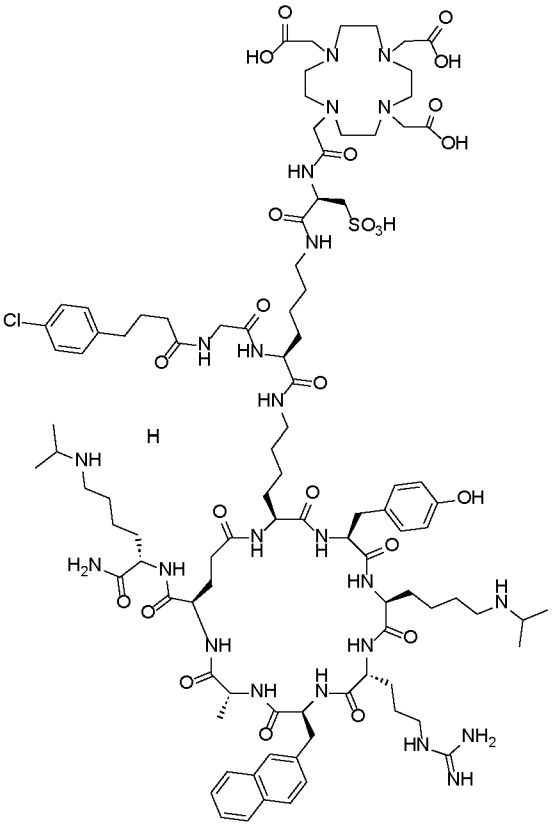
;



;

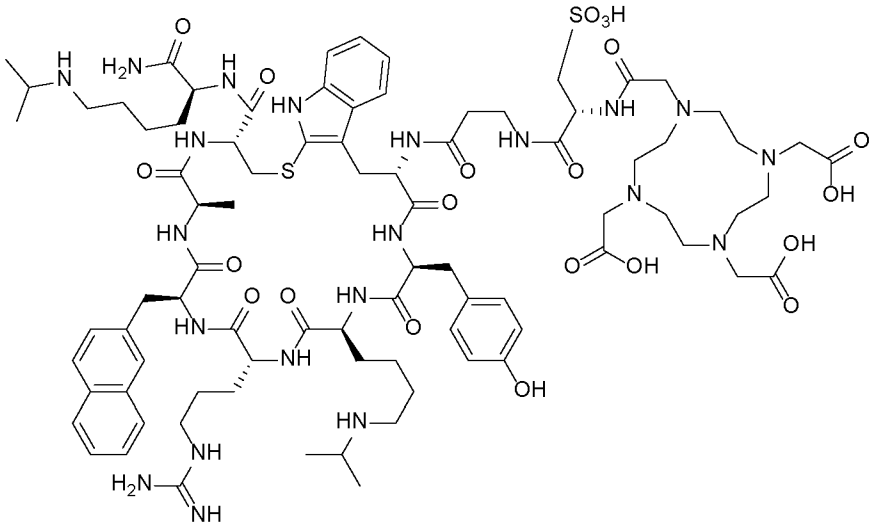


;

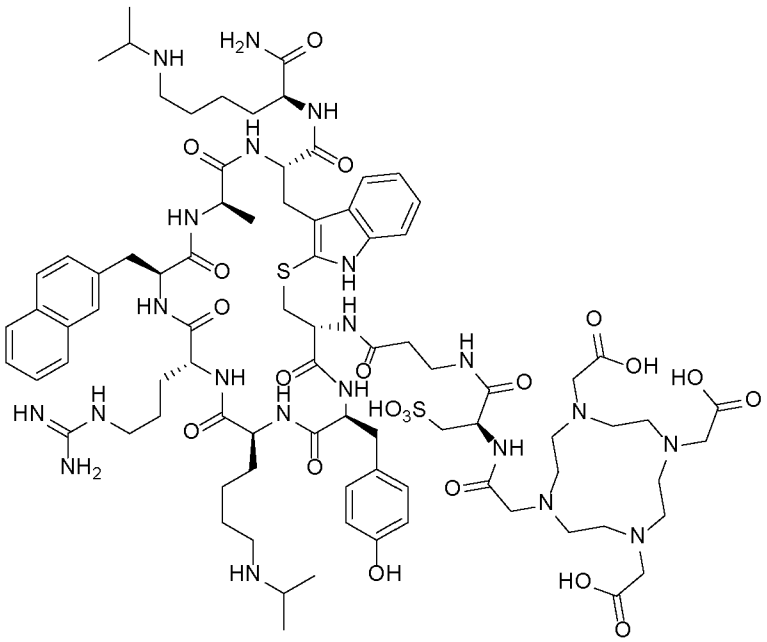


, or salt or solvate thereof.

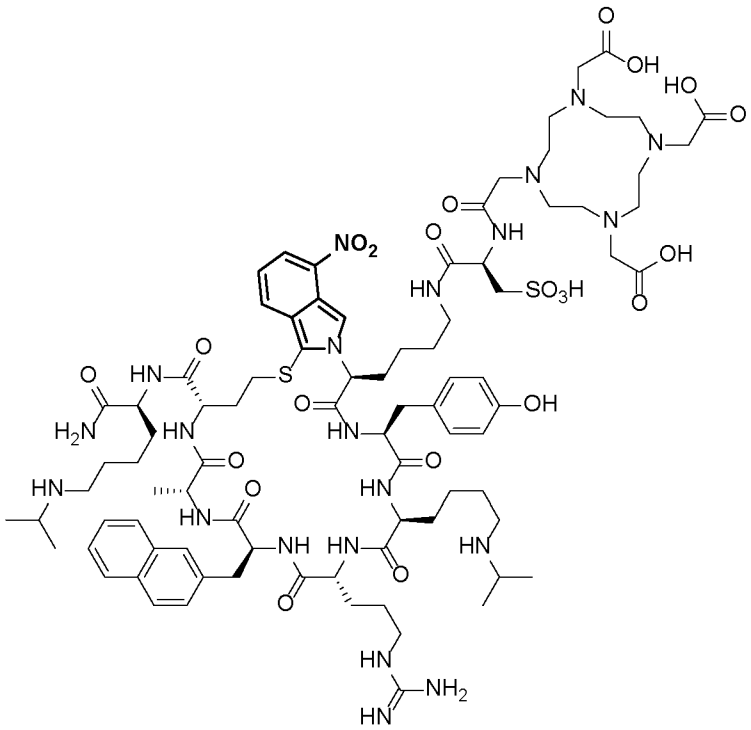
133. The compound of claim 1 of Formula B having the following chemical formula:



;

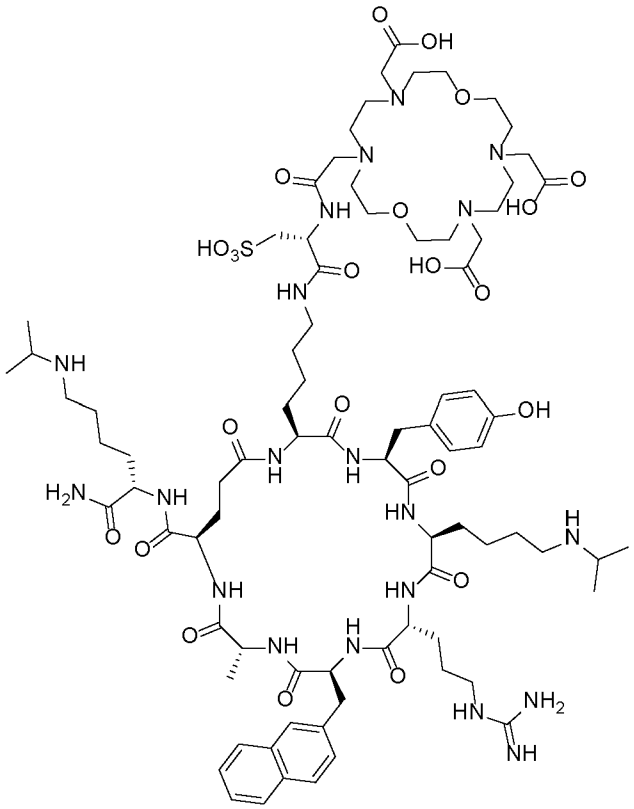


or



, or salt or solvate thereof.

134. A compound having the following chemical formula:



, or salt or solvate thereof.

135. The compound of any one of claims 1-134, for use in imaging a CXCR4-expressing tissue in a subject or for imaging an inflammatory condition or disease, wherein at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope.

136. The compound of claim 135, wherein the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I, ^{152}Tb, ^{155}Tb, or ^{72}As.

137. The compound of any one of claims 1-136, for use in imaging a CXCR4-expressing tissue in a subject or for imaging an inflammatory condition or disease, wherein the compound is bound to a metal chelator complexed with an imaging radioisotope, optionally through a linker; or the compound is bound to a prosthetic group containing BF_3 comprising at least one ^{18}F, optionally through a linker.

138. The compound of claim 137, wherein the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{131}I, ^{123}I, ^{124}I, ^{152}Tb, ^{155}Tb, or ^{72}As.

139. The compound of any one of claims 1-134, for use in treating a disease or condition characterized by expression of CXCR4 in a subject, wherein at least one R^X comprises a therapeutic radioisotope or is complexed with a therapeutic radioisotope, or at least one R^X comprises a therapeutic moiety.

140. The compound of any one of claims 1-134, for use in treating a disease or condition characterized by expression of CXCR4 in a subject, wherein the compound is bound to a metal chelator complexed with a therapeutic radioisotope, optionally through a linker.

141. The compound of claim 139 or 140, wherein the therapeutic radioisotope is ^{165}Er, ^{212}Bi, ^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu, ^{111}In, ^{213}Bi, ^{212}Pb, ^{47}Sc, ^{90}Y, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac, ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu, or ^{67}Cu.

142. The compound of any one of claims 139-141, wherein the disease or condition is a CXCR4-expressing cancer.

143. A method of imaging a CXCR4-expressing tissue, comprising administering an effective amount of the compound of any one of claims 137-138 to a subject in need of such imaging.

144. A method of treating a disease or condition characterized by expression of CXCR4 in a subject, comprising administering an effective amount of the compound of any one of claims 139-142 to a subject in need thereof.

145. The method of claim 144, wherein the disease or condition is a CXCR4-expressing cancer.

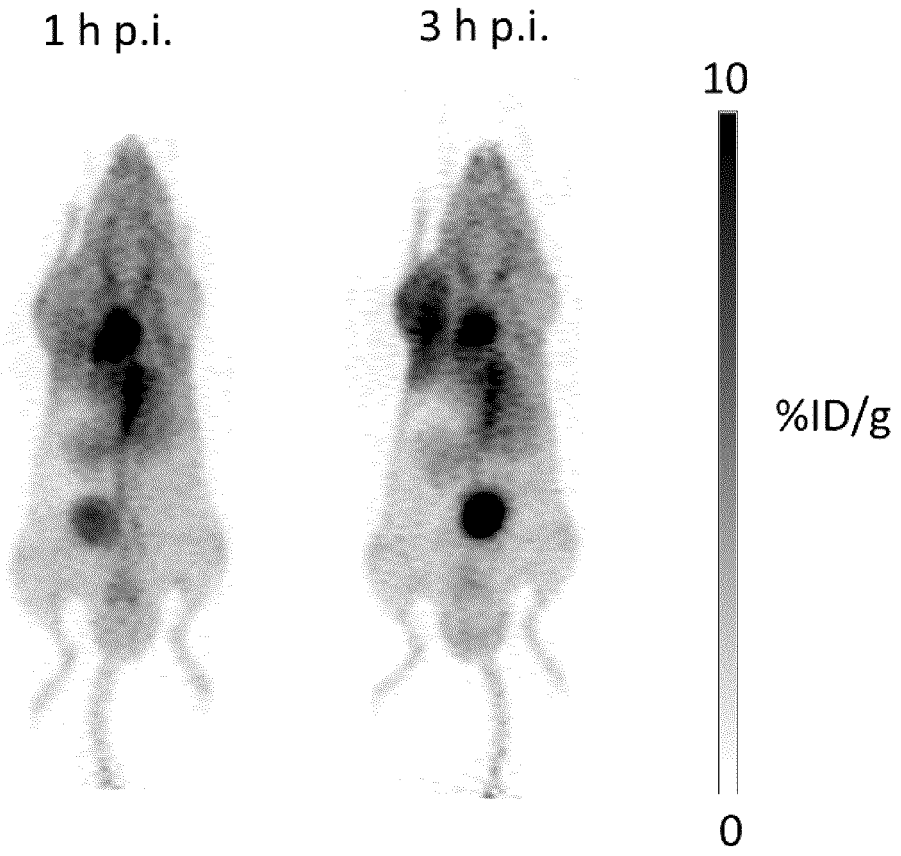


FIG. 1

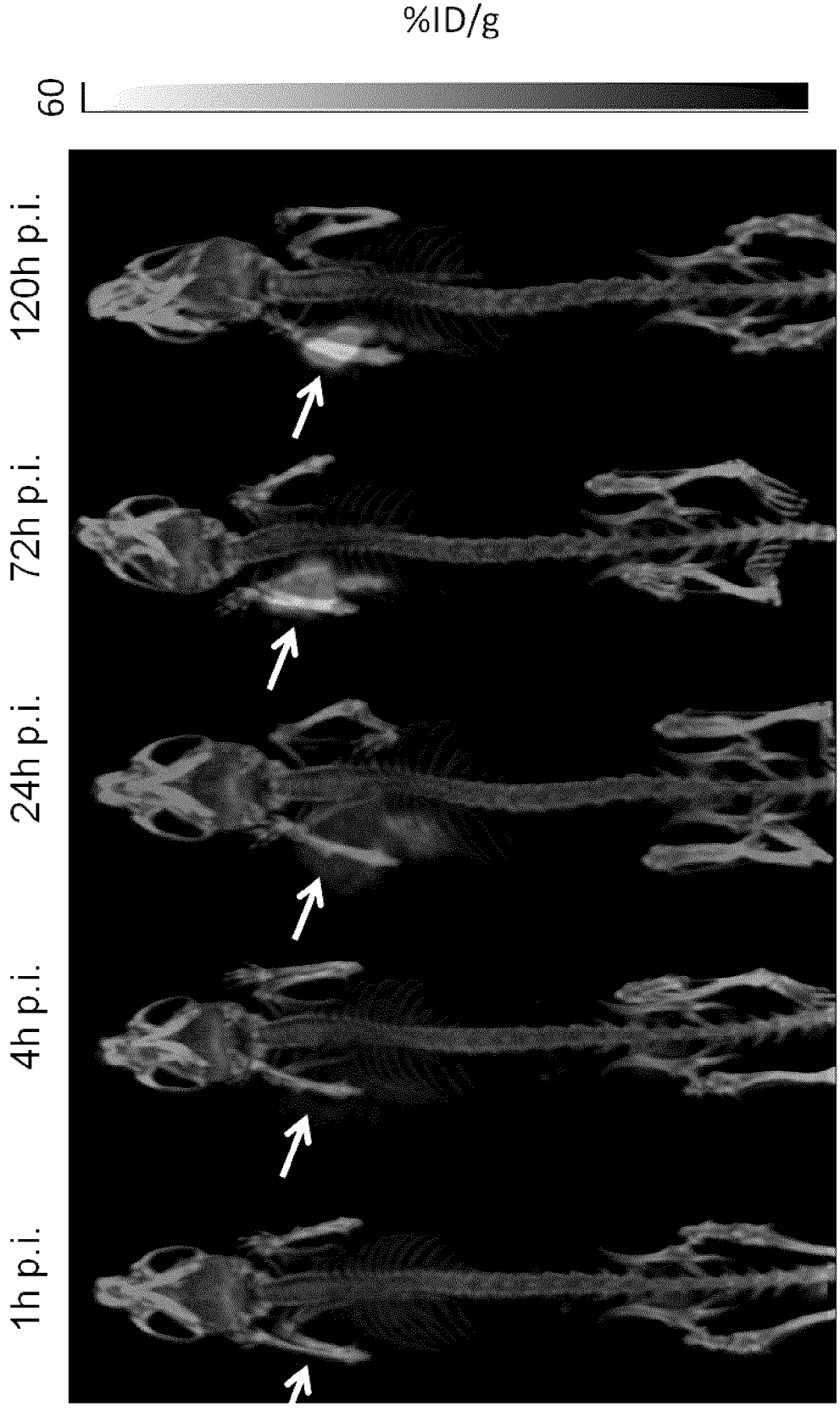


FIG. 2

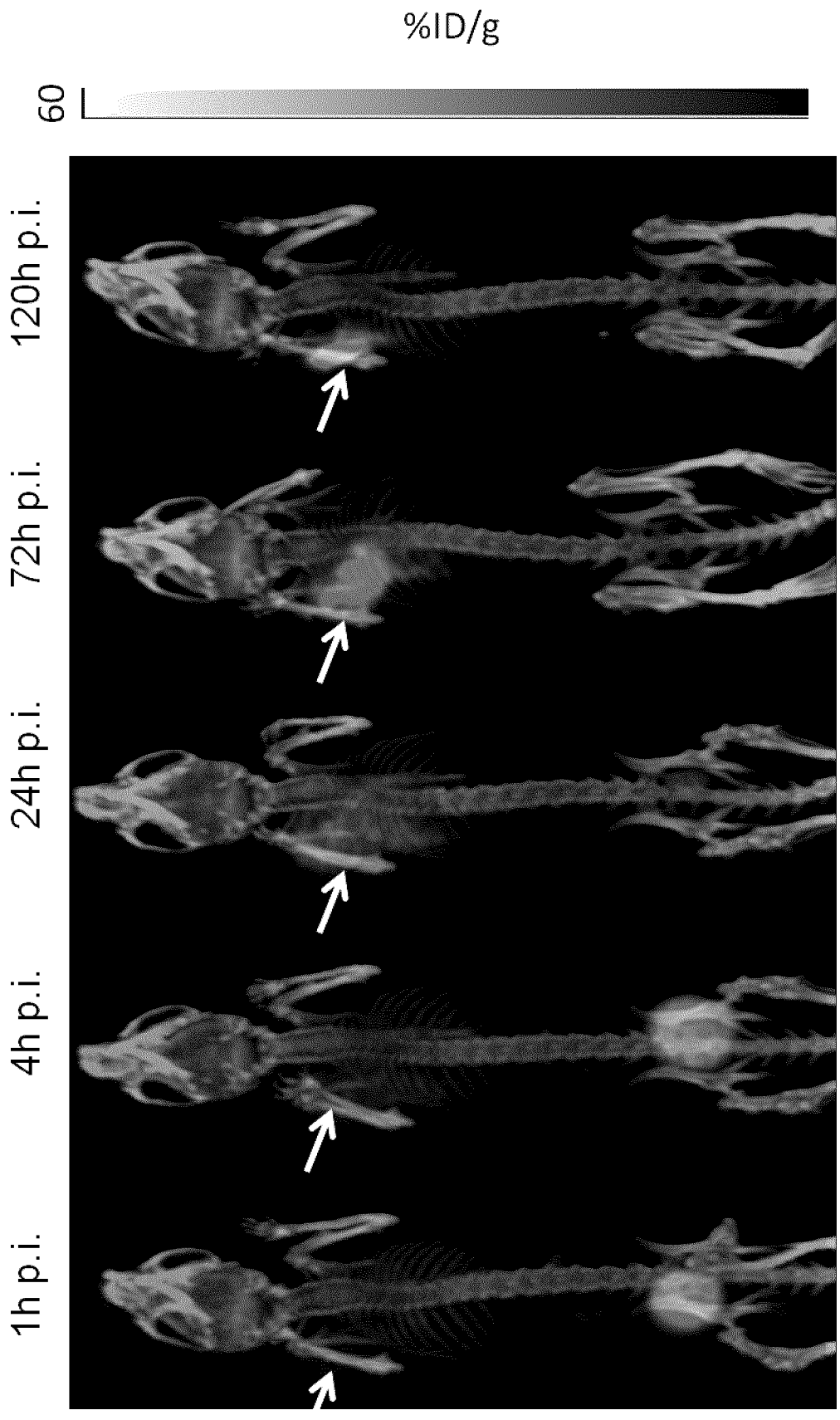


FIG. 3

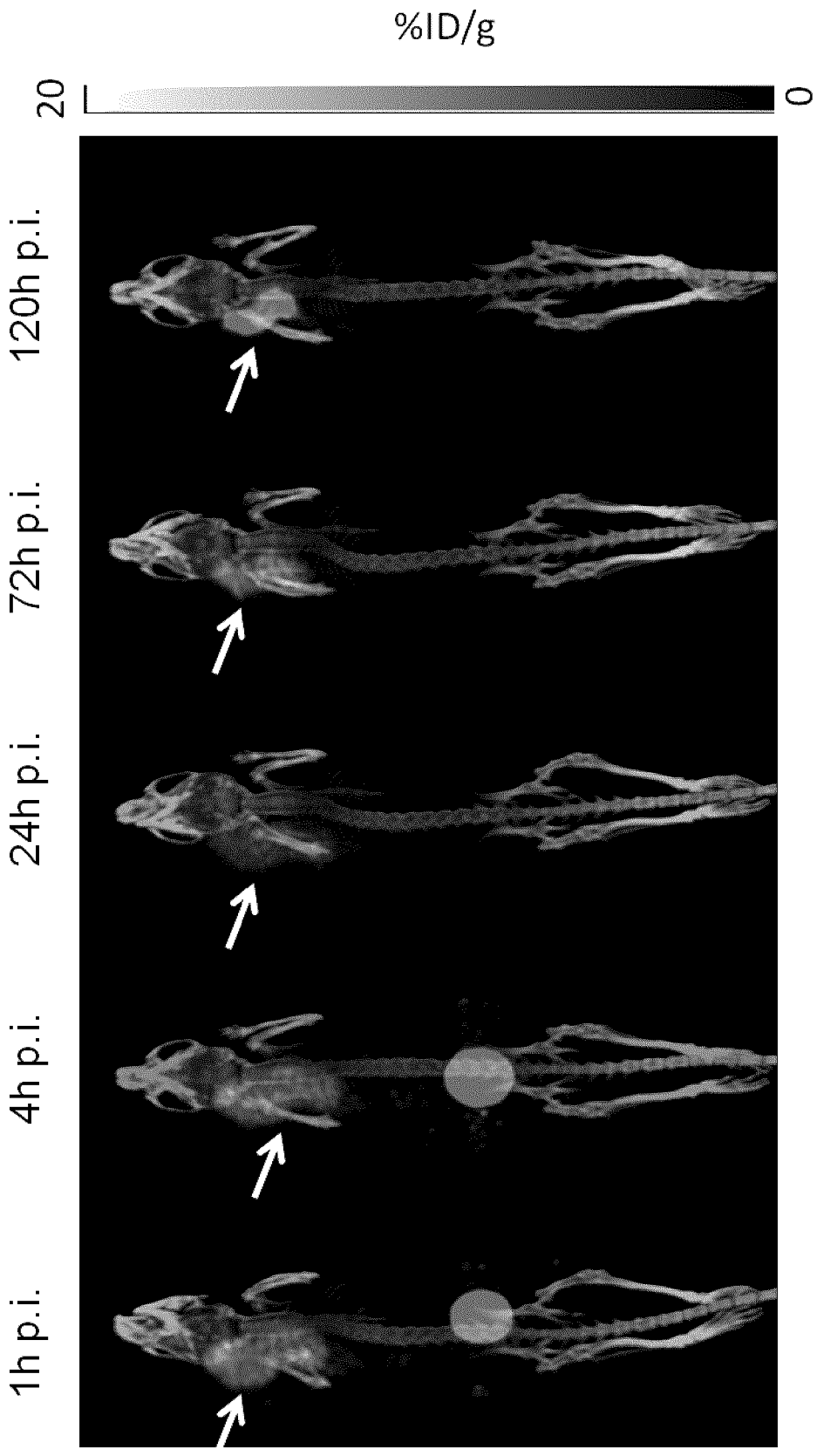


FIG. 4

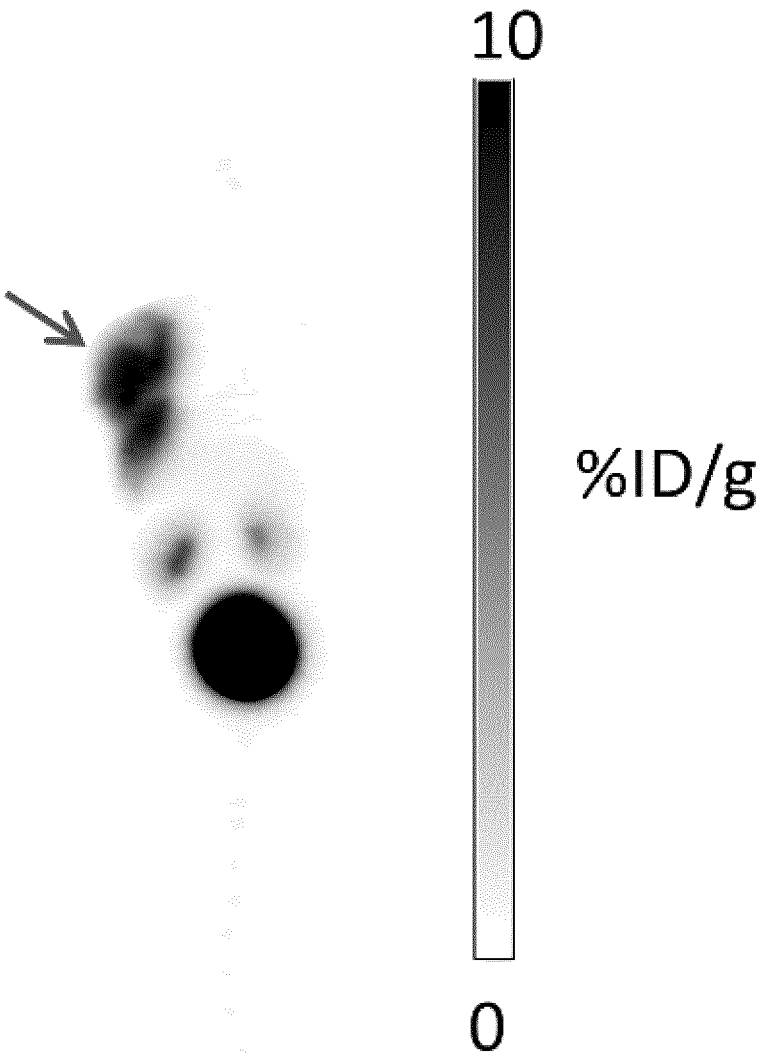


FIG. 5

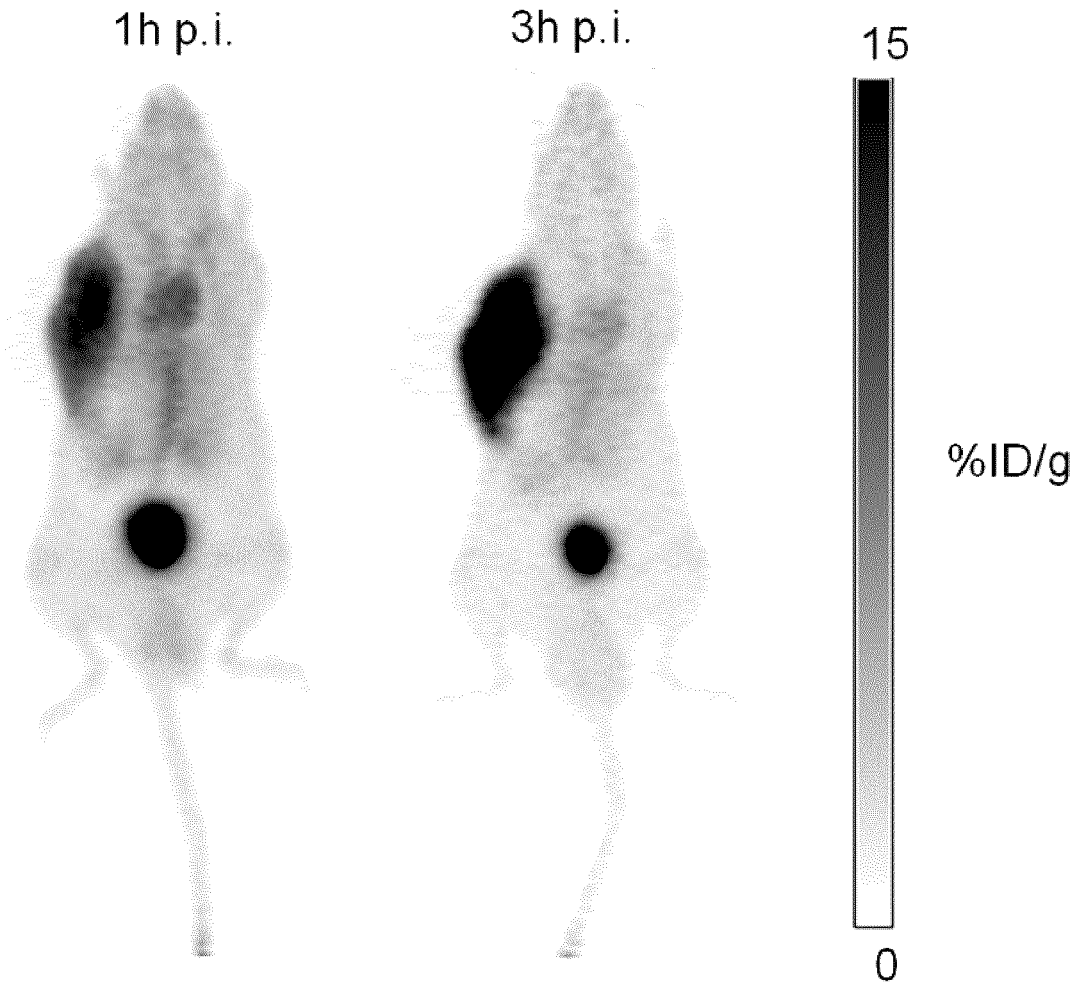


FIG. 6

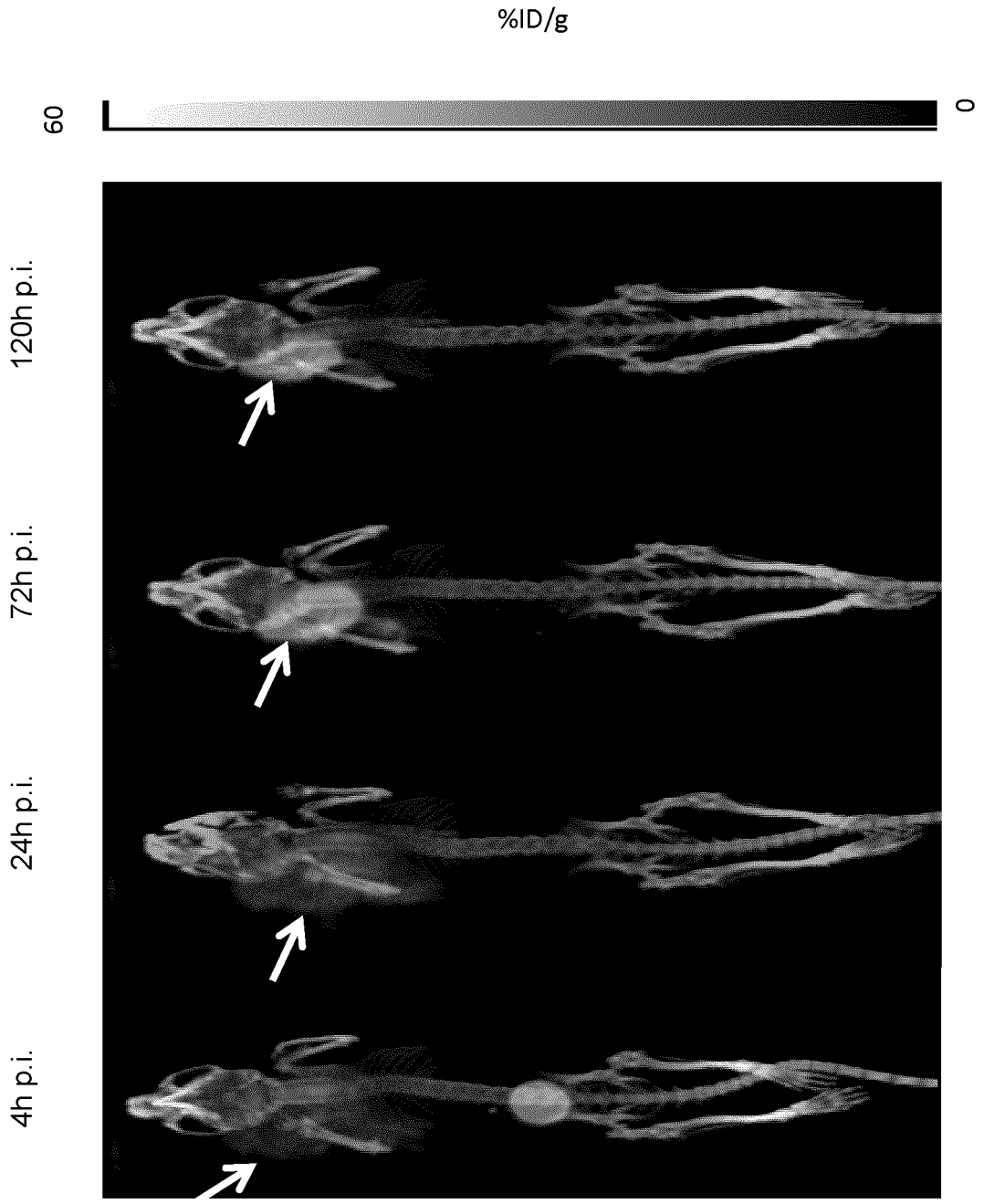


FIG. 7

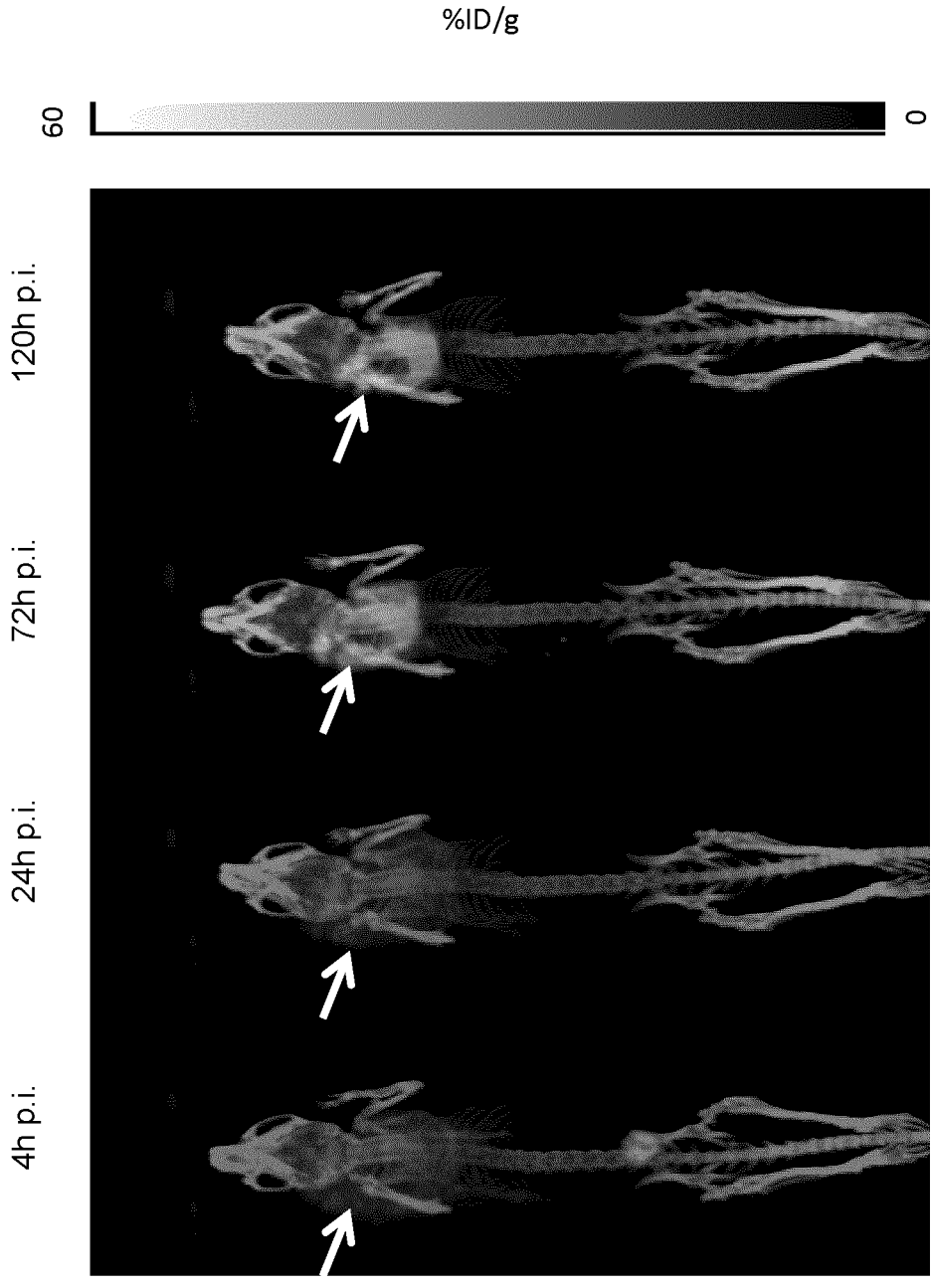


FIG. 8