Supporting Information

Harki *et al.* 10.1073/pnas.0806308105

SI Experimental Details

^{18}F-Radiosynthesis. ***General.*** No carrier-added [^{18}F]-fluoride was produced by the ^{18}O(p,n)^{18}F nuclear reaction via 11 MeV proton bombardment of ^{18}O-enriched H_2O (95%) in an RDS-112 cyclotron. Anhydrous and bulk solvents were obtained from Sigma-Aldrich. Preparative HPLC purification was performed on a KNAUER HPLC system equipped with a KNAUER UV detector (254 nm), a Carroll & Ramsey Associates γ-radiation detector, and a Phenomenex Gemini C-18 column (250 × 10 mm, 5 μm). The mobile phase for preparative HPLC purification used an isocratic elution (5 ml/min flow rate) of 60:40 MeOH:TFA (0.1% aqueous) for polyamide **1** and 65:35 MeOH:TFA (0.1% aqueous) for polyamide **3**. Analytical HPLC analysis was performed on a KNAUER HPLC system equipped with a KNAUER UV detector (254 nm), a Carroll & Ramsey Associates γ-radiation detector, and an Alltech Altima C-18 column (250 × 4.6 mm, 5 μm). The mobile phase for analytical HPLC analysis used an isocratic elution (2 ml/min flow rate) of 60:40 MeOH:TFA (0.1% aqueous) for polyamide **1** and 75:25 MeOH:TFA (0.1% aqueous) for polyamide **3** (at 1 ml/min flow rate). *Important note:* MeOH was used in place of acetonitrile (MeCN) to prevent radiolysis of ^{18}F-labeled polyamides (data not shown). SPE used Waters C-18 Sep-Pak cartridges. The identity of [^{18}F]-labeled products were verified by analytical HPLC analysis of coinjected samples spiked with the corresponding fluorine-19 standard **2** or **4** (Fig. S3). Specific activity measurements were performed by analytical HPLC analysis (γ-radiation) of [^{18}F]-labeled material against a UV-generated (254 nm) standard curve from the corresponding fluorine-19 standard. EtOH and sterile saline for *in vivo* injection were purchased from Gold Shield Chemicals and Hospira, Inc., respectively.

4-[^{18}F]-fluorobenzaldehyde (6). This compound was prepared by modification of the previously reported procedures (1–3). In brief, cyclotron-produced [^{18}F]-fluoride (421 mCi) was added to a reaction vessel containing Kryptofix [2.2.2] (10 mg, 0.026 mmole) and K_2CO_3 (1 mg, 0.007 mmole). The material was dehydrated by azeotropic distillation with MeCN, and then added to a solution of (4-formylphenyl) trimethylammonium triflate (4) (**5**, 5 mg, 0.016 mmol) in DMSO (0.7 ml) followed by heating at 100°C for 10 min. The reaction mixture was then diluted with excess H_2O and loaded onto an SPE cartridge. The cartridge was washed with HCl (0.1 N aqueous, 10 ml), H_2O (15 ml), and dried with a stream of N_2 for 2 min. For polyamide conjugation, the material was eluted with MeOH (0.7 ml) and used immediately. For *in vivo* injection and subsequent PET/CT analysis (Fig. S2) the material was eluted from the SPE cartridge with EtOH (1.0 ml) and diluted with saline. The radiochemical yield (decay-corrected) following SPE was 385 mCi (91% yield, decay-corrected) at ≈60 min after EOB.

Polyamide 1. A solution of polyamide **8** (1 μmole) in MeOH (100 μl) was combined with TFA (2.5% aqueous, 100 μl) and aniline (5) (1.0 M soln in MeOH, 2 μl, 2.0 μmoles) and added to 4-[^{18}F]-fluorobenzaldehyde (**6**) eluted from the SPE cartridge (in 0.7 ml MeOH). The solution was mixed by N_2 bubbling, then heated in a closed system to 100°C for 20 min. The reaction was cooled briefly, diluted with excess H_2O and purified by preparative HPLC. The radiochemical yield of **1** following HPLC purification was 29.0 mCi (12% yield decay-corrected) at ≈100 min after EOB. For *in vivo* injection, purified polyamide **1** was extracted from the HPLC eluant by loading onto a SPE cartridge, washing with excess H_2O, and eluting with EtOH (0.3 ml fractions were collected). Ethanolic fractions containing polyamide **1** were diluted with normal saline for *in vivo* experiments.

Polyamide 3. A solution of polyamide **9** (1 μmole) in MeOH (100 μl) was combined with NH_4OAc (0.1 M aqueous, 100 μl) and aniline (5) (1.0 M soln in MeOH, 2 μl, 2.0 μmoles) and added to 4-[^{18}F]-fluorobenzaldehyde (**6**) eluted from the SPE cartridge (in 0.7 ml MeOH). The solution was mixed by N_2 bubbling, then heated in a closed system to 100°C for 20 min. The reaction was cooled briefly, diluted with excess H_2O and purified by preparative HPLC. The radiochemical yield of polyamide **3** following HPLC purification was 20.4 mCi (7% yield decay-corrected) at ≈100 min after EOB. The specific activity of polyamide **3** was determined to be >2,000 Ci/mmole at EOB. For *in vivo* injection, purified **3** was extracted from the HPLC eluant by loading onto a SPE cartridge, washing with excess H_2O, and eluting with EtOH (1.5 ml). The ethanolic fraction containing polyamide **3** was concentrated to ≈0.1 ml by vacuum and nitrogen bubbling at 50°C and diluted with normal saline for *in vivo* experiments.

Synthesis of Fluorine-19 Standards and Radiolabeling Precursors. ***General.*** Anhydrous *N*,*N*-dimethylformamide (DMF), diisopropylethylamine (DIEA), triethylsilane (Et_3SiH), trifluoroacetic acid (TFA), piperidine, aqueous ammonium acetate (NH_4OAc, ≈5M), 4-fluorobenzaldehyde (**7**), and 3-chlorothiophene-2-carboxylic acid (**21**) were purchased from Sigma-Aldrich. Kaiser oxime resin (LL, 200–400 mesh) and benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate (PyBOP) were from Novabiochem. *t*-Butyloxycarbonyl-β-alanine-pam resin (0.4–0.7 meq/g) and 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) were purchased from Peptides International. *N*-α-Boc-*N*-γ-Fmoc-D-diaminobutyric acid [Boc-D-Dab(Fmoc)-OH] was purchased from Bachem. Bulk grade solvents were from Fisher Scientific. Thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} coated plates. Preparative HPLC purification was performed on either a Beckman Gold or Agilent 1200 Series instrument equipped with a Phenomenex Gemini preparative column (250 × 21.2 mm, 5 μm) with the mobile phase consisting of a gradient of acetonitrile (MeCN) in 0.1% TFA (aqueous). Analytical HPLC analysis was conducted on a Beckman Gold instrument equipped with a Phenomenex Gemini analytical column (250 × 4.6 mm, 5 μm), a diode array detector, and the mobile phase consisting of a gradient of MeCN in 0.1% TFA (aqueous). Polyamide concentrations were measured by UV analysis on a Hewlett-Packard model 8453 diode array spectrophotometer in 20% MeCN in distilled and deionized water (ddH_2O) with a molar extinction coefficient (ε) of 43,125 $M^{-1}cm^{-1}$ at a wavelength (λ_{max}) of ≈290 nm for β-linked polyamides (**2**, **8**, and **11**), and ε = 69,500 $M^{-1}cm^{-1}$ at λ_{max} ≈315 nm for hairpin polyamides (**4** and **9**). Addition of the oxime-linked 4-fluorobenzaldehyde label to either polyamide scaffold did not influence the molar extinction (ε) values. High-resolution mass spectrometry was performed on a Waters Acquity UPLC-LCT Premiere XE TOF-MS (ESI^+) system. NMR spectroscopy was performed on a Varian instrument operating at either 300 or 500 MHz (for ^{1}H). Chemical shifts are reported in parts per million relative to the internal solvent peak or tetramethylsilane for spectrum obtained in $CDCl_3$.

Synthesis of β-Linked Polyamides. Resin-bound polyamide **10** was synthesized on Boc-β-alanine PAM resin using established protocols (6). The hydroxylamine-functionalized polyamide **8** was prepared by the sequence shown in Scheme S1.

Polyamide 11. An aliquot of resin **10** (143.8 mg, 82.7 μmoles theoretical yield) was swelled in DMF (2 ml), treated with aqueous LiOH (1M, 2 ml), and then heated in a sealed vial at 55°C for 13 h. The resin was filtered, washed with MeCN (2 ml) and DMF (2 ml), and the filtrate was neutralized with aqueous HCl (1N, 2 ml). The filtrate was diluted with distilled water (to 20 ml), purified by preparative RP-HPLC, and then lyophilized to yield polyamide **11** (25.21 μmoles, 30% recovery). HRMS (ESI^+) calculated for $C_{36}H_{44}N_{15}O_9$ $[M+H]^+$ 830.3446, found 830.3454.

Polyamide 8. To a solution of polyamide **11** (45.10 μmoles) in DMF (1 ml) was added PyBOP (76.1 mg, 146.2 μmoles) and DIEA (78.6 μl, 451.2 μmole). The reaction was shaken at 37°C for 20 min, then *tert*-butyl-3-aminopropoxycarbamate (**12**, 104.8 mg, 550.9 μmoles) (7) in DMF (1 ml) was added, and the reaction was shaken at 37°C for an additional 40 min. The crude reaction products were diluted with aqueous trifluoroacetic acid (0.1% TFA, 6 ml), purified by RP-HPLC, and lyophilized to dryness to provide the Boc-protected hydroxylamine (28.61 μmoles, 63% yield). An aliquot of this material (23.24 μmoles) was deprotected by dissolving in CH_2Cl_2 containing TFA and Et_3SiH (79:20:1 CH_2Cl_2:TFA:Et_3SiH, 10 ml). The solution was allowed to stand at RT for 20 min, then diluted with MeOH (5 ml) and concentrated *in vacuo*. The residual material was redissolved in MeCN:MeOH (2:1, 3 ml) and diluted with aqueous trifluoroacetic acid (0.1% TFA, to 9 ml). Purification by RP-HPLC followed by lyophilization provided polyamide **8** (14.00 μmoles, 60% yield). HRMS (ESI^+) calculated for $C_{39}H_{52}N_{17}O_9$ $[M+H]^+$ 902.4134, found 902.4163.

Polyamide 2. Polyamide **8** (4.63 μmoles) was dissolved in DMF (340 μl) and NH_4OAc (0.1 M aqueous, 500 μl), then 4-fluorobenzaldehyde (**7**, 100 mM soln in DMF, 160 μl) was added. The reaction was shaken at 40°C for 40 min, and then diluted with a solution of MeCN in aqueous trifluoroacetic acid (20% MeCN in 0.1% TFA, 7 ml). Purification by RP-HPLC followed by lyophilization provided polyamide **2** (2.25 μmoles, 49% yield). It should be noted that although oximes can exist as *E*- and *Z*-isomers, analytical HPLC analysis of the crude reaction products revealed one major product. The remaining peaks with retention times proximal to **2** were minor in abundance (≤ 11% peak area compared with **2**) and not characterized. Polyamide **2** was assigned the *E*- configuration based on the ^1H NMR chemical shift (data not shown) of the oxime methine proton (δ 8.23 in DMSO-d_6) in comparison to a structurally similar *O*-alkyl 4-fluorobenzaldehyde-oxime (*E*-isomer, δ 8.02 in CD_3OD) (3), and that methine protons of *E*-oximes resonate at appreciably lower fields than corresponding *Z*-isomers (8). HRMS (ESI^+) calculated for $C_{46}H_{55}N_{17}O_9F$ $[M+H]^+$ 1008.4353, found 1008.4360.

Synthesis of Hairpin Polyamides. Hairpin polyamide **13** (Scheme S2) was synthesized on Kaiser oxime resin using established protocols (9), except more complicated amino acid building blocks were used to reduce the number of on-resin couplings. In brief, following loading of the first pyrrole amino acid according to published protocol (9), trimer **19** (synthesis shown in Scheme S3) was installed yielding the complete bottom strand of polyamide **13**. The chiral turn was introduced by coupling of α-Boc-*N*-γ-Fmoc-D-diaminobutyric acid, thereby yielding the chiral α-amine protected as a *t*-butyl carbamate (Boc) and the terminal γ-amino group Fmoc-protected. Removal of the Fmoc with 25% piperidine in DMF, followed by coupling with tetramer **23** (synthesis shown in Scheme S4) provided polyamide **13**. The hydroxylamine-functionalized polyamide **9** was prepared by the sequence shown in Scheme S2.

Polyamide 9. An aliquot of resin **13** (75.1 mg, 30.6 μmoles theoretical yield) was treated with *tert*-butyl-3-aminopropoxycarbamate (**12**, 266 mg, 1.40 mmoles) (7) dissolved in DMF (1 ml) and shaken at 55°C for 15 h. The resin was then filtered, washed with DMF (2 ml) and MeCN (2 ml), and the eluant diluted with aqueous trifluoroacetic acid (0.1% TFA, 5 ml). Purification by RP-HPLC followed by lyophilization yielded the resin-cleaved, Boc-protected polyamide. Both carbamate protecting groups were removed by dissolving the residual material in CH_2Cl_2 containing TFA and Et_3SiH (79:20:1 CH_2Cl_2:TFA:Et_3SiH, 2 ml). The solution was allowed to stand at room temperature for 20 min, then diluted with MeOH (4 ml) and concentrated *in vacuo*. The residual material was redissolved in MeCN (2 ml), and diluted with aqueous trifluoroacetic acid (0.1% TFA, to 9 ml). Purification by RP-HPLC followed by lyophilization provided polyamide **9** (2.98 μmoles, 10% recovery). HRMS (ESI^+) calculated for $C_{52}H_{60}ClN_{20}O_{10}S$ $[M+H]^+$ 1191.4211, found 1191.4178.

Polyamide 4. Polyamide **9** (1.21 μmoles) was dissolved in DMF (195 μl) and NH_4OAc (0.1 M aqueous, 200 μl), and then 4-fluorobenzaldehyde (**7**, 1.0 M soln in DMF, 5 μl) was added. The reaction was shaken at 40°C for 50 min, and then diluted with a solution of MeCN in aqueous trifluoroacetic acid (20% MeCN in 0.1% TFA, 7 ml). Purification by RP-HPLC followed by lyophilization provided polyamide **4** (500 nmoles, 41% yield). Analytical HPLC analysis of the crude reaction products revealed only one major product. The remaining peaks with retention times proximal to polyamide **4** were minor in abundance (≤ 11% peak area compared with **4**) and not characterized. Polyamide **4** was assigned the *E*- configuration based on studies with related polyamide **2**. HRMS (ESI^+) calculated for $C_{59}H_{64}ClFN_{20}O_{10}S$ $[M+H]^+/2$ 649.2254, found 649.2223; $C_{59}H_{63}ClFN_{20}O_{10}S$ $[M+H]^+$ 1297.4429, found 1297.4049.

Ethyl 4-(4-(tert-butoxycarbonylamino)-1-methylpyrrole-2-carboxamido)-1-methylimidazole-2-carboxylate (16). To a solution of **14** (9.35 g, 45.47 mmole) (6) and **15** (14.47 g, 40.49 mmole) (6) in DMF (100 ml) was added DIEA (21.0 ml, 120.6 mmole), and the solution was stirred at 50°C for 2 d. The product was precipitated in distilled H_2O (1.5 L), filtered, and washed with excess distilled H_2O. The residual solid was dissolved in $CHCl_3$ (400 ml), washed with brine (100 ml, 1×), dried over $MgSO_4$ and concentrated *in vacuo*. The residual oil was redissolved in ethyl acetate (≈50 ml) and precipitated by addition of hexanes (≈400 ml). The white solid was collected, washed with additional hexanes, and dried *in vacuo* to yield dimer **16** (12.51 g, 79% yield) as a white solid. TLC (3:2 ethyl acetate:hexanes) R_f 0.46; ^1H NMR (499.8 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.54 (s, 1H), 7.09 (s, 1H), 6.34 (d, J = 1.7 Hz, 1H), 6.32 (s, 1H), 4.41 (q, J = 7.1 Hz, 2 H), 4.01 (s, 3H), 3.92 (s, 3H), 1.50 (s, 9H), 1.43 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 158.8, 158.3, 153.1, 137.1, 131.4, 122.03, 121.97, 119.3, 114.5, 103.0, 80.3, 61.5, 36.8, 36.0, 28.3, 14.4; HRMS (ESI^+) calculated for $C_{18}H_{26}N_5O_5$ $[M+H]^+$ 392.1934, found 392.1919.

4-(4-(tert-butoxycarbonylamino)-1-methylpyrrole-2-carboxamido)-1-methylimidazole-2-carboxylic acid (17). To a solution of dimer **16** (1.460 g, 3.730 mmole) in MeOH (7 ml) was added aqueous LiOH (1 M, 7 ml). The solution was shaken at 37°C for 16 h, then neutralized with aqueous HCl (1 N, 7 ml) yielding a precipitate. The solid was collected by filtration, washed with excess distilled H_2O, then dried *in vacuo* to yield **17** (1.150 g, 85% yield). Spectral data matches that which has been previously reported (6).

4-(4(4-(tert-butoxycarbonylamino)-1-methylpyrrole-2-carboxamido)-1-methylimidazole-2-carboxamido)-1-methylpyrrole-2-carboxylic acid (19). A solution of **17** (1.010 g, 2.78 mmole), PyBOP (1.320 g, 2.54 mmole), and DIEA (2.4 ml, 13.78 mmole) in DMF (7 ml) was shaken at 37°C for 25 min. Next, amine **18** (1.034 g, 5.42 mmole) (6) was added, and the reaction was shaken at 37°C for 20 h. The reaction was then poured into distilled H_2O (200 ml) and extracted with ethyl acetate (500 ml, 1×). The organic layer was washed with aqueous citric acid (1 M, 250 ml, 1×), brine (250 ml, 1×), then dried over Na_2SO_4 and concentrated *in vacuo*. The residual material was redissolved in DMF/MeOH/MeCN and precipitated by addition of excess distilled H_2O. This precipita-

tion step was repeated (1×) by redissolving the solid in MeCN/MeOH followed by precipitation from distilled H_2O. The residual solid was suspended in MeCN/distilled H_2O, frozen, and lyophilized to dryness. The resulting trimer was saponified by dissolving in 1,4-dioxane (8 ml) followed by addition of aqueous LiOH (1 M, 5 ml). The solution was shaken at 37°C for 20 h, and then neutralized by addition of aqueous HCl (1 N, 5 ml). The resulting white precipitate was diluted with excess distilled H_2O and collected by centrifugation. The pelleted solid was suspended in MeCN (15 ml), precipitated by addition of excess distilled H_2O, and again collected by centrifugation (this step was performed 2×). The resulting white solid was suspended in MeCN:distilled H_2O (≈1:1), frozen, and lyophilized to dryness to yield **19** (469 mg, 38% yield). ^{1}H NMR (300.1 MHz, DMSO-d_6): δ 10.12 (s 1H), 10.09 (s, 1H), 9.10 (s, 1H), 7.51 (s, 1H), 7.46 (d, J = 1.8 Hz, 1H), 6.98 (s, 1H), 6.92 (d, J = 1.8 Hz, 1H), 6.84 (m, 1H), 3.95 (s, 3H), 3.82 (s, 3H), 3.80 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (125.7 MHz, DMSO-d_6): δ 162.0, 158.7, 155.8, 152.9, 136.1, 134.0, 122.5, 122.0, 121.8, 120.4, 119.8, 117.9, 114.8, 108.7, 104.7, 78.4, 36.3, 36.2, 35.0, 28.2; HRMS (ESI$^+$) calc'd for $C_{22}H_{28}N_7O_6$ $[M+H]^+$ 486.2101, found 486.2086.

Ethyl 4-(4-(4-(tert-butoxycarbonylamino)-1-methylpyrrole-2-carboxamido)-1-methylpyrrole-2-carbox-amido)-1-methylimidazole-2-carboxylate (20). Dimer **16** (1.869 g, 4.77 mmole) was dissolved in CH_2Cl_2 containing TFA and Et_3SiH (79:20:1 CH_2Cl_2:TFA:Et_3SiH, 30 ml) and stirred at room temperature for 20 min. The reaction was concentrated *in vacuo*, redissolved in MeOH (20 ml) and concentrated *in vacuo* again (repeated 2×). To the residual brown solid was added **15** (1.762 g, 4.93 mmole) and the solids were dissolved in DMF (15 ml) with DIEA (5.0 ml, 28.70 mmole). The reaction was heated to 50°C for 48 h. The crude reaction products were precipitated by addition of distilled H_2O (500 ml), filtered, and washed with excess distilled H_2O. The resulting brown solid was dissolved in $CHCl_3$ (300 ml), washed with brine (200 ml, 1×), dried over Na_2SO_4 and concentrated *in vacuo* followed by drying under high vacuum to yield trimer **20** (2.183 g, 89% yield). TLC (19:1 CH_2Cl_2: MeOH) R_f 0.32; ^{1}H NMR (499.8 MHz, DMSO-d_6): δ 10.77 (s, 1H), 9.89 (s, 1H), 9.12 (s, 1H), 7.67 (s, 1H), 7.34 (d, J = 1.7 Hz, 1H), 7.09 (d, J = 1.7 Hz, 1H), 6.89 (s, 1H), 6.85 (s, 1H), 4.26 (q, J = 7.1 Hz, 2 H), 3.93 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 1.44 (s, 9H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, DMSO-d_6): δ 158.8, 158.6, 158.5, 152.9, 137.9, 130.8, 122.8, 122.34, 122.26, 121.7, 119.7, 117.0, 115.5, 105.8, 103.9, 78.3, 60.6, 36.4, 36.1, 35.5, 28.2, 14.2; HRMS (ESI$^+$) calculated for $C_{24}H_{32}N_7O_6$ $[M+H]^+$ 514.2414, found 514.2417.

Ethyl 4-(4-(4-(3-chlorothiophene-2-carboxamido)-1-methylpyrrole-2-carboxamido)-1-methylpyrrole-2-carboxamido)-1-methylimidazole-2-carboxylate (22). Trimer **20** (540 mg, 1.05 mmole) was dissolved in CH_2Cl_2 containing TFA and Et_3SiH (19:80:1 CH_2Cl_2:TFA:Et_3SiH, 5 ml) and stirred at room temperature for 20 min. MeOH (20 ml) was added and the reaction was concentrated *in vacuo*. The residual material was triturated (2×) by being redissolved in MeOH (20 ml) and concentrating *in vacuo*, then dried briefly under high vacuum. Separately, chlorothiophene **21** (262 mg, 1.61 mmole) and PyBOP (832 mg, 1.60 mmole) were dissolved in DMF (4 ml) and DIEA (2.2 ml, 12.93 mmole) and shaken at 37°C for 30 mins. The deprotected amine, which was dissolved in DMF (5 ml), was added to this material and the reaction was shaken at 37°C for 20 h. The crude product was then precipitated by addition to distilled H_2O (40 ml) and the brown solid was collected by centrifugation (this precipitation sequence was repeated 2×). The resulting solid was suspended in ethyl acetate:hexanes (1:1, 400 ml), filtered, and the solid was dried *in vacuo* to provide tetramer **22** (258 mg, 44% yield). TLC (19:1 CH_2Cl_2: MeOH) R_f 0.23; ^{1}H NMR (300.1 MHz, DMSO-d_6): δ 10.75 (s, 1H), 10.21 (s, 1H), 9.99 (s, 1H), 7.85 (d, J = 5.0 Hz, 1H), 7.67 (s, 1H), 7.36 (d, J = 1.9 Hz, 1H), 7.29 (d, J = 1.9 Hz, 1H), 7.17 (d, J = 5.3 Hz, 1H), 7.10 (d, J = 1.9 Hz, 1H), 7.06 (d, J = 1.9 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2 H), 3.93 (s, 3H), 3.86 (s, 3H), 3.85 (2, 3H), 1.29 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125.7 MHz, DMSO-d_6): δ 158.8, 158.6, 158.4, 157.0, 137.9, 131.6, 130.8, 129.0, 128.9, 124.1, 123.0, 122.2, 121.8, 121.2, 119.7, 118.9, 115.5, 105.7, 104.9, 60.6, 36.4, 36.2, 35.5, 14.2; HRMS (ESI$^+$) calculated for $C_{24}H_{25}ClN_7O_5S$ $[M+H]^+$ 558.1326, found 558.1318.

4-(4-(4-(3-chlorothiophene-2-carboxamido)-1-methylpyrrole-2-carboxamido)-1-methylpyrrole-2-carbox-amido)-1-methylimidazole-2-carboxylic acid (23). Tetramer **22** (224 mg, 0.401 mmole) was suspended in 1,4-dioxane (6 ml) and aqueous LiOH (1 M, 6 ml), then shaken at 37°C for 19 h. The residual solution was added to distilled H_2O (30 ml), neutralized by addition of aqueous HCl (1 N, 6 ml), and the resulting solid was collected by centrifugation. The precipitated solid was washed by suspending in distilled H_2O (30 ml), then collected by centrifugation. The resulting brown solid was suspended in distilled H_2O (30 ml), frozen, and lyophilized to dryness yielding tetramer **23** (204 mg, 96% yield). ^{1}H NMR (300.1 MHz, DMSO-d_6): δ 10.53 (s, 1H), 10.23 (s, 1H), 10.02 (s, 1H), 7.85 (d, J = 5.3 Hz, 1H), 7.40 (s, 1H), 7.36 (d, J = 1.6 Hz, 1H), 7.30 (d, J = 1.6 Hz, 1H), 7.21 (s, 1H), 7.17 (d, J = 5.3 Hz, 1H), 7.06 (d, J = 1.6 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 161.0, 158.5, 158.4, 157.0, 136.1, 131.5, 128.9, 128.8, 124.1, 123.1, 122.2, 122.0, 121.2, 119.5, 119.0, 112.7, 105.7, 104.9, 36.2, 34.9; HRMS (ESI$^+$) calculated for $C_{22}H_{21}ClN_7O_5S$ $[M+H]^+$ 530.1013, found 530.1009.

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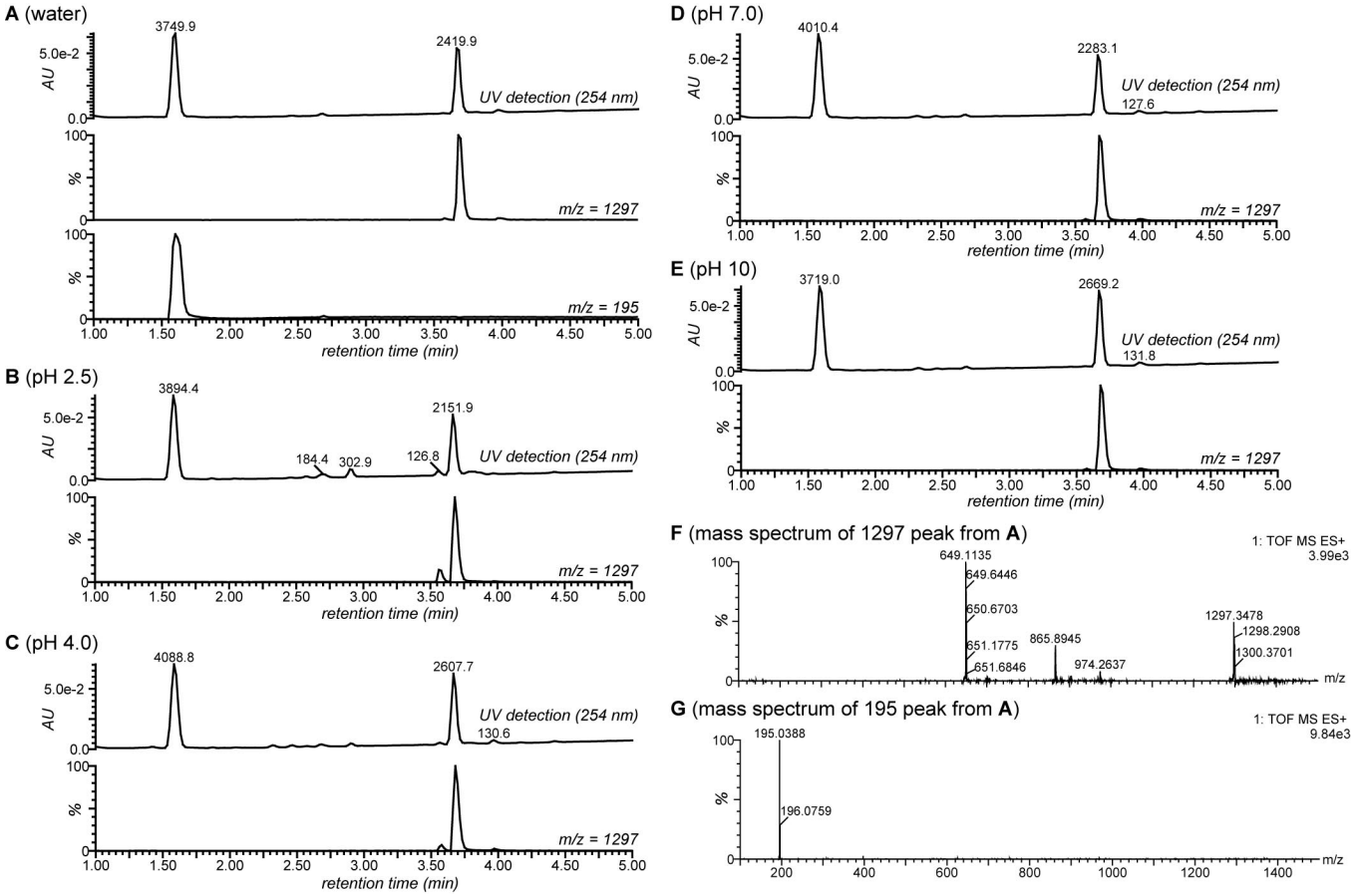


Fig. S1. UPLC-MS analysis of polyamide **4**. Polyamide **4** was incubated at 37°C for 4 h in distilled and deionized water (*A*), pH 2.5 buffer (*B*), pH 4.0 buffer (*C*), pH 7.0 buffer (*D*), and pH 10 buffer (*E*), then neutralized with aqueous NH_4OAc containing 9-aminoacridine as a standard. DMI (15%, vol/vol) was used as a cosolvent for both the incubation and neutralization steps. UV chromatograms (*A–E*) are detection at 254 nm. Mass detection of $m/z = 1,297$ (*A–E*; mass of **4**) and 195 (only shown for *A*; mass of 9-aminoacridine) was performed for each sample. (*F*) Mass spectrum of the 1,297 peak shown in *A*. (*G*) Mass spectrum of the 195 peak shown in *A*.

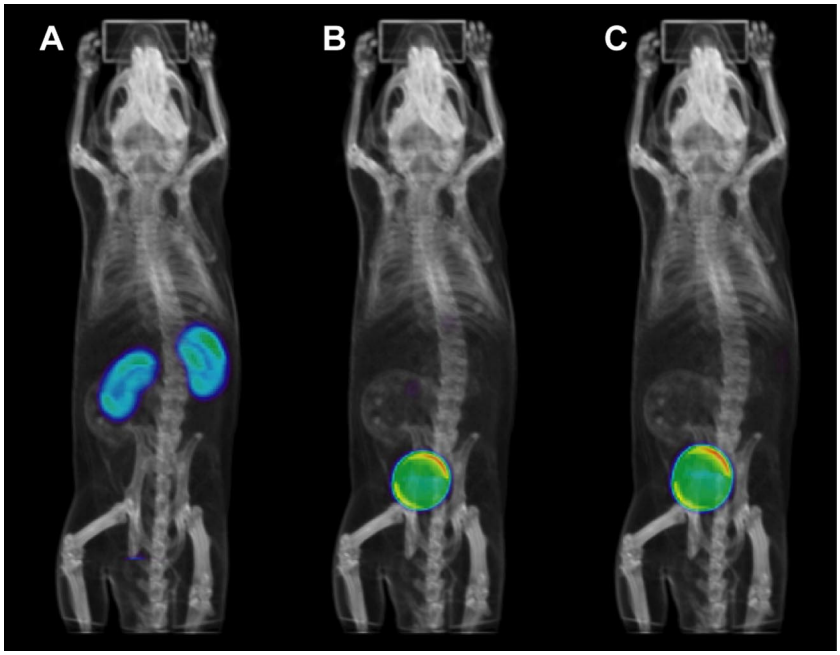


Fig. S2. PET/CT images of a 4-[^{18}F]-fluorobenzaldehyde (**6**) dosed mouse. (*A*) One minute after injection showing rapid kidney uptake. (*B*) Thirty minutes after injection showing residual kidney occupancy and mostly bladder localization. (*C*) Two hours after injection showing the dose primarily in the bladder.

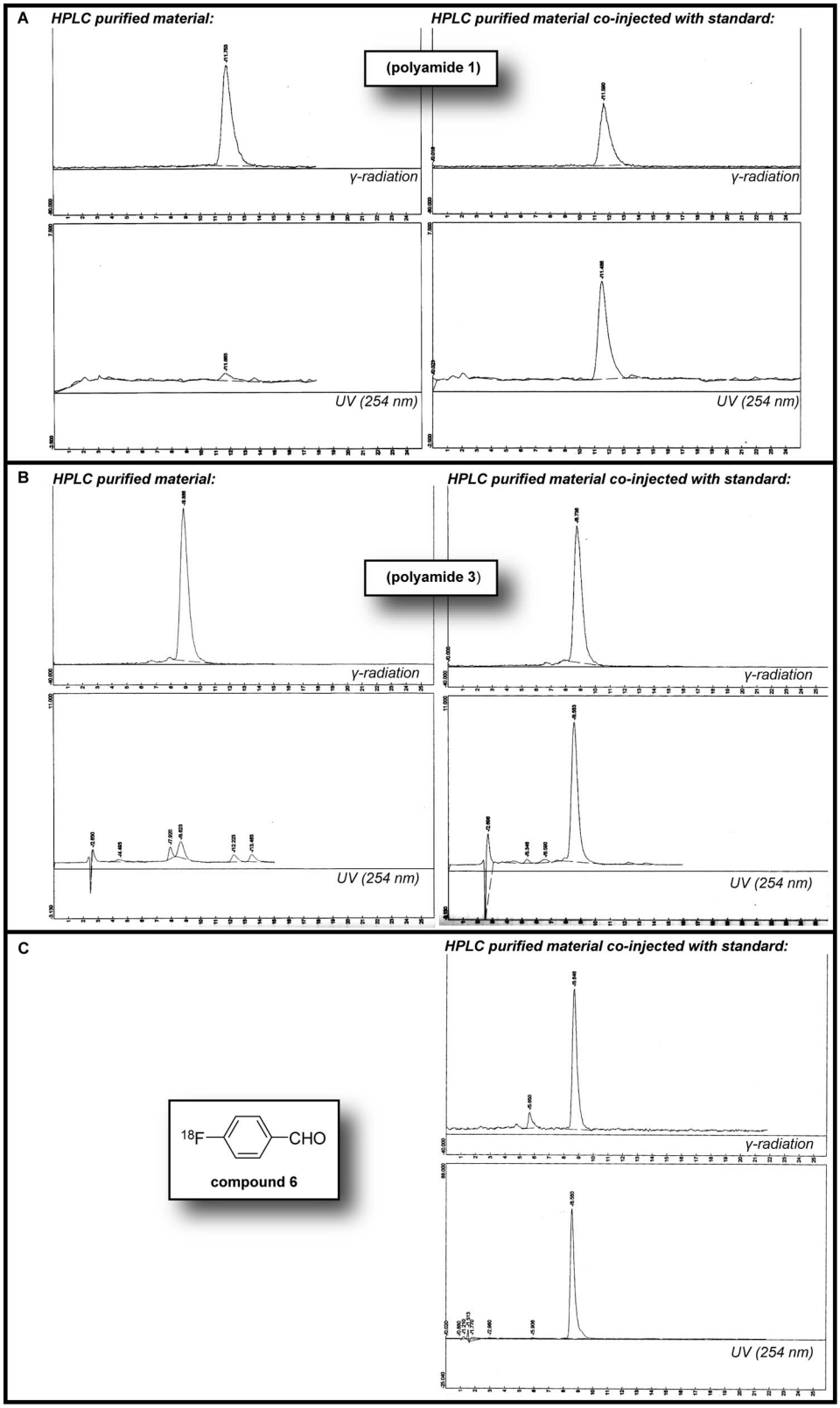
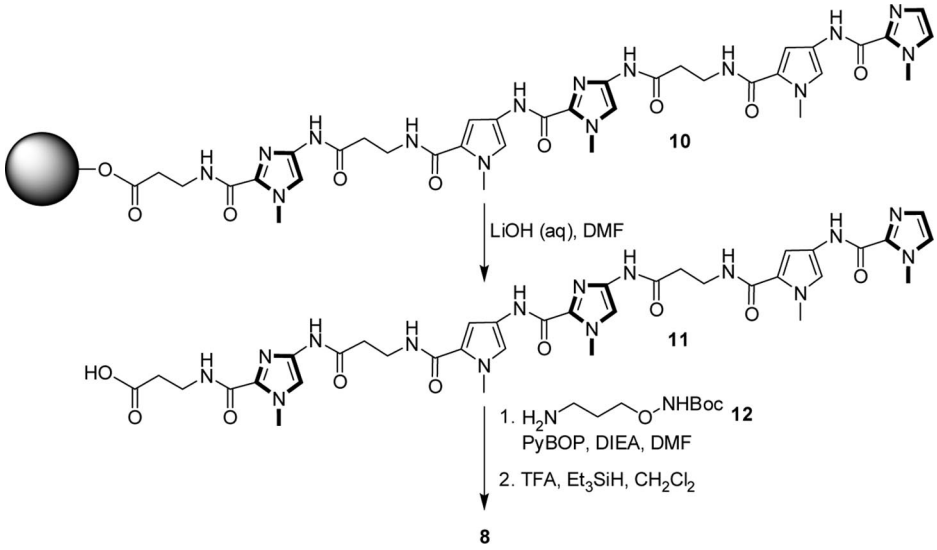
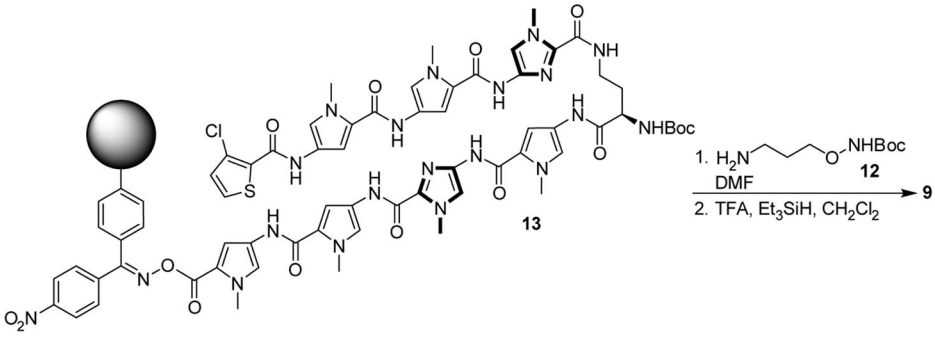


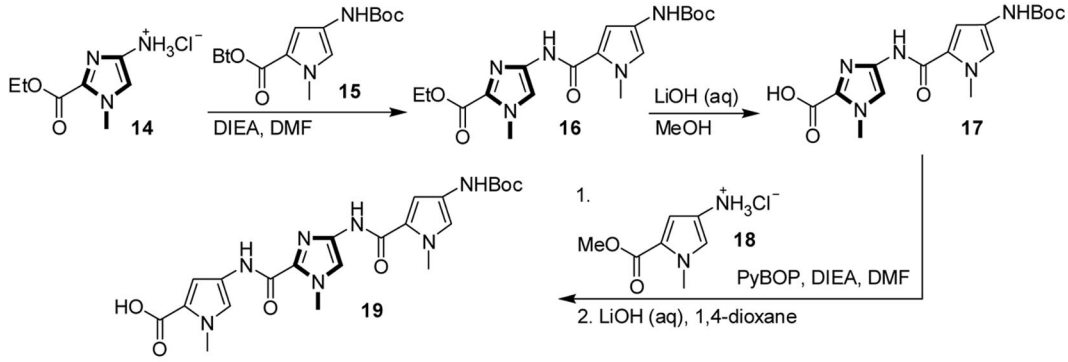
Fig. S3. Analytical HPLC analysis of ^{18}F-labeled material (*left column*) and samples coinjected with their corresponding fluorine-19 standards (*right column*). (*A*) Polyamide **1**, (*B*) polyamide **3**, (*C*) 4-[^{18}F]-fluorobenzaldehyde (**6**) following solid phase extraction (SPE) elution.



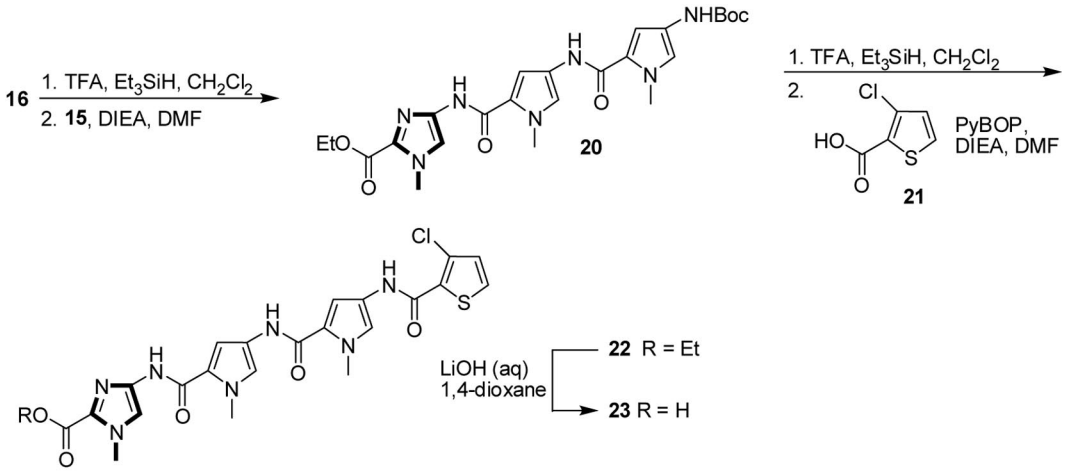
Scheme S1. Synthesis of β-linked polyamide **8**.



Scheme S2. Synthesis of hairpin polyamide **9**.



Scheme S3. Synthesis of trimer **19**.



Scheme S4. Synthesis of tetramer **23**.

Table S1. Details of PET/CT experiments conducted in this study

^{18}F-labeled compound	Session ID	Mouse ID	Injected activity	Scan duration, h
4-fluorobenzaldehyde **6**	m20832	9165	492 μCi	3
β-linked **1**	m20279	8885	472 μCi	3
β-linked **1**	m20414	8885	218 μCi	2
β-linked **1**	m20415	8972	193 μCi	2
hairpin **3**	m21366	9447	543 μCi	2
hairpin **3**	m21367	9448	191 μCi	2
hairpin **3**	m21401	9457	84 μCi	2

Session and mouse ID are tracking information used by the Crump Preclinical Imaging Center at UCLA to identify the mouse and specific imaging experiment.

Table S2. Dosimetry data for 1

Target organ	m20279	m20414	m20415	Average	SD, %
Adrenals	4.45E-02	4.70E-02	4.01E-02	4.39E-02	8
Brain	3.37E-03	3.68E-03	4.24E-03	3.76E-03	12
Breasts	1.43E-02	1.57E-02	1.60E-02	1.53E-02	6
Gallbladder wall	3.06E-01	3.82E-01	2.71E-01	3.20E-01	18
Lower large intestine wall	2.02E-02	8.77E-02	9.47E-02	6.75E-02	61
Small intestine	7.07E-02	8.78E-01	8.39E-01	5.96E-01	76
Stomach wall	2.53E-02	4.66E-02	4.51E-02	3.90E-02	30
Upper large intestine wall	3.66E-02	1.79E-01	1.72E-01	1.29E-01	62
Heart wall	3.29E-02	3.06E-02	2.69E-02	3.01E-02	10
Kidneys	1.40E-01	6.93E-02	6.76E-02	9.23E-02	45
Liver	3.33E-01	2.92E-01	1.87E-01	2.71E-01	28
Lungs	2.37E-02	2.44E-02	2.26E-02	2.36E-02	4
Muscle	1.76E-02	3.09E-02	3.29E-02	2.71E-02	31
Ovaries	2.39E-02	1.21E-01	1.25E-01	9.00E-02	64
Pancreas	4.15E-02	5.27E-02	4.66E-02	4.69E-02	12
Red marrow	1.88E-02	3.84E-02	3.89E-02	3.20E-02	36
Osteogenic cells	2.12E-02	3.02E-02	3.33E-02	2.82E-02	22
Skin	1.17E-02	1.64E-02	1.80E-02	1.54E-02	21
Spleen	2.04E-02	2.96E-02	3.05E-02	2.68E-02	21
Testes	1.26E-02	2.16E-02	2.90E-02	2.11E-02	39
Thymus	1.53E-02	1.63E-02	1.75E-02	1.64E-02	7
Thyroid	1.12E-02	1.24E-02	1.50E-02	1.29E-02	15
Urinary bladder wall	1.27E-01	3.62E-01	6.19E-01	3.69E-01	67
Uterus	2.70E-02	1.20E-01	1.34E-01	9.37E-02	62
Total body	2.65E-02	4.58E-02	4.45E-02	3.89E-02	28

Organs values are rem/mCi; nuclide: ^{18}F (1.10E02 min).

Table S3. Dosimetry data for 3

Target organ	m21366	m21367	m21401	Average	SD, %
Adrenals	6.72E-02	6.20E-02	6.48E-02	6.47E-02	4
Brain	1.53E-02	1.43E-02	1.32E-02	1.43E-02	7
Breasts	3.08E-02	3.05E-02	3.22E-02	3.12E-02	3
Gallbladder wall	4.04E-01	1.86E-01	7.92E-02	2.23E-01	74
Lower large intestine wall	1.48E-01	1.53E-01	1.30E-01	1.44E-01	8
Small intestine	1.24E-01	1.25E-01	1.10E-01	1.20E-01	7
Stomach wall	5.10E-02	4.91E-02	5.05E-02	5.02E-02	2
Upper large intestine wall	1.28E-01	1.28E-01	1.13E-01	1.23E-01	7
Heart wall	6.37E-02	5.82E-02	5.97E-02	6.05E-02	5
Kidneys	4.88E-01	3.63E-01	3.88E-01	4.13E-01	16
Liver	2.05E-01	1.92E-01	2.00E-01	1.99E-01	3
Lungs	4.08E-02	4.01E-02	4.22E-02	4.10E-02	3
Muscle	3.92E-02	3.90E-02	3.95E-02	3.92E-02	1
Ovaries	5.97E-02	6.14E-02	5.66E-02	5.92E-02	4
Pancreas	6.57E-02	6.05E-02	6.23E-02	6.28E-02	4
Red marrow	4.10E-02	4.01E-02	4.08E-02	4.06E-02	1
Osteogenic cells	5.50E-02	5.50E-02	5.75E-02	5.58E-02	3
Skin	2.86E-02	2.85E-02	2.97E-02	2.89E-02	2
Spleen	5.23E-02	4.88E-02	5.12E-02	5.08E-02	4
Testes	3.47E-02	3.62E-02	3.50E-02	3.53E-02	2
Thymus	3.71E-02	3.67E-02	3.88E-02	3.75E-02	3
Thyroid	3.35E-02	3.38E-02	3.59E-02	3.44E-02	4
Urinary bladder wall	1.39E-01	1.95E-01	4.56E-02	1.27E-01	60
Uterus	5.76E-02	6.11E-02	5.20E-02	5.69E-02	8
Total Body	4.65E-02	4.54E-02	4.60E-02	4.60E-02	1

Organs values are rem/mCi; nuclide: ^{18}F (1.10E02 min).