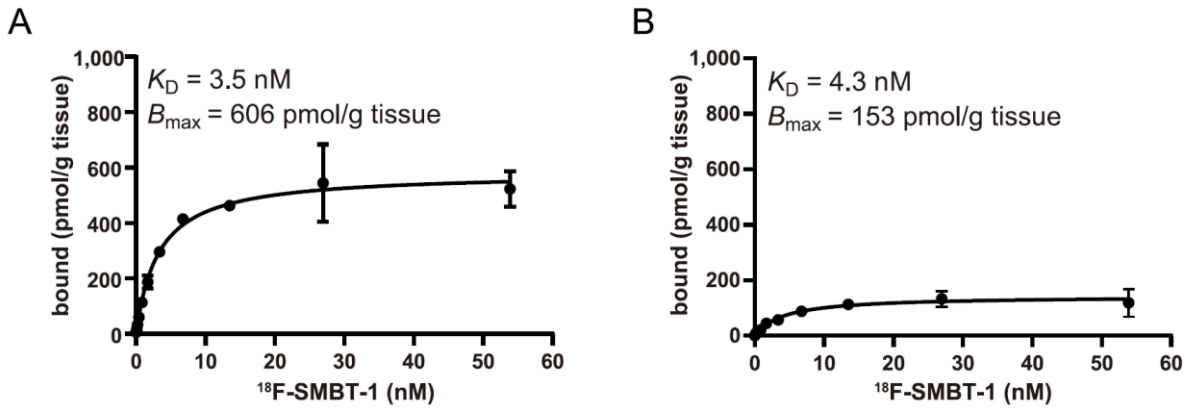
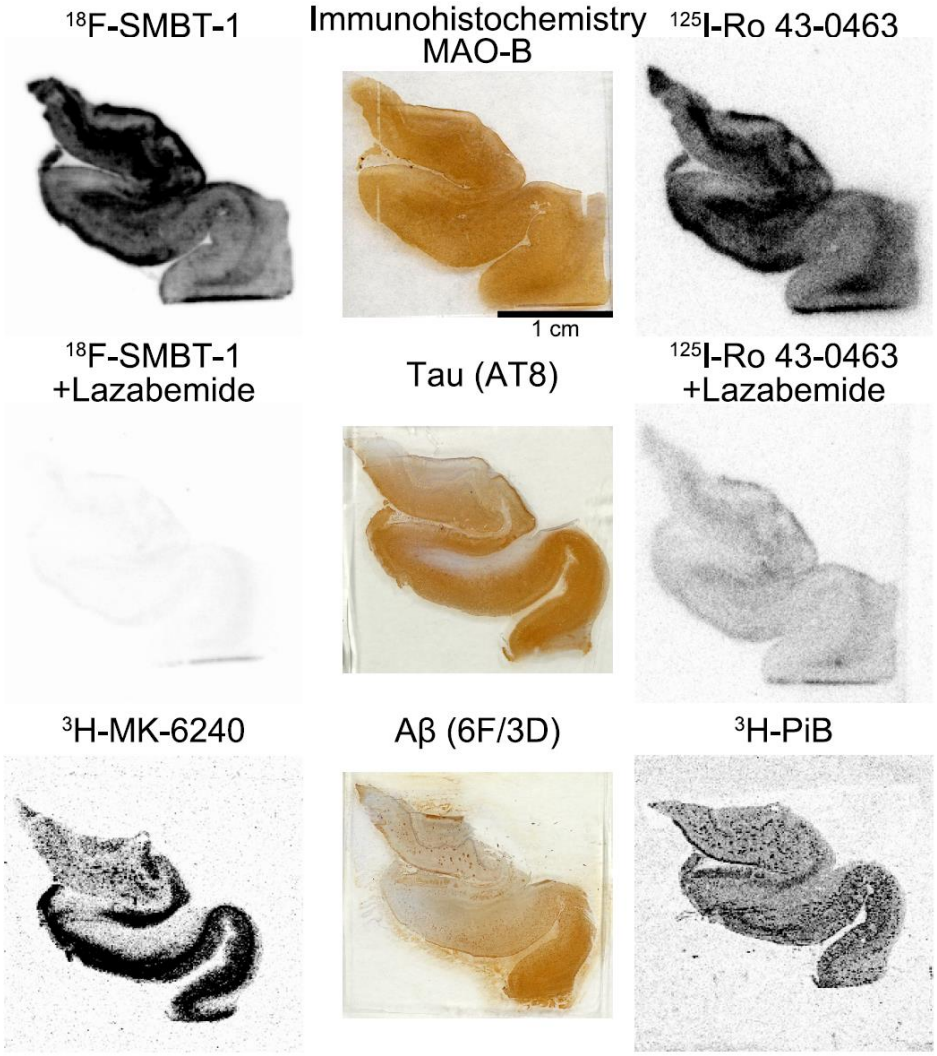



**Supplemental Figure 1: *In vitro* saturation binding of $^{18}$F-SMBT-1 against (A) human brain homogenates (Alzheimer's disease, 81-year-old male) and (B) mouse brain homogenates (C57BL/6, 12-month male).**

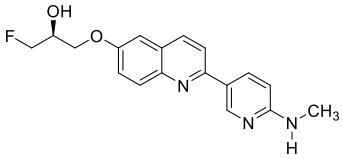
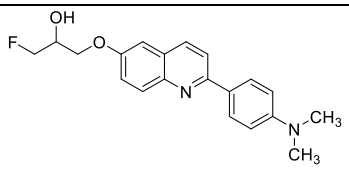
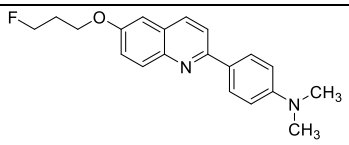
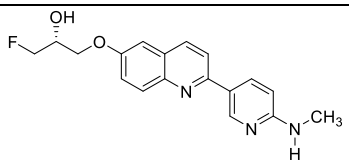
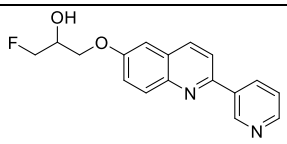
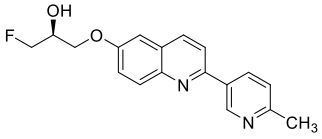
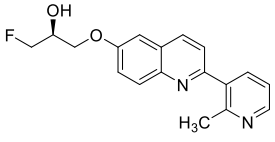


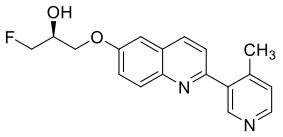
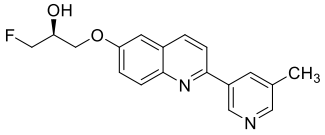
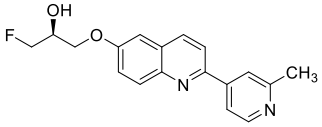
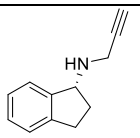
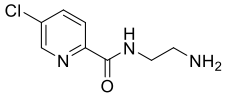
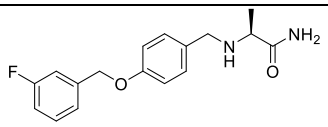

**Supplemental Figure 2: Comparative *in vitro* autoradiography of $^{18}$F-SMBT-1, $^{125}$I-Ro 43-0463, $^{3}$H-MK-6240, and $^{3}$H-PiB in the hippocampal section of a patient with Alzheimer's disease (81-year male). Adjusted sections were stained by anti- monoamine oxidase-B (MAO-B), anti-pTau (AT8), and anti-amyloid-β (6F/3D) antibodies.**

**Supplemental Table 1 Summary of the procedure and conditions for radiosynthesis of $^{18}$F-SMBT-1.**

| Steps | Operations | Conditions |
|---|---|---|
| 1 | $^{18}F^-$ elution from QMA-C | Krypt222 (8 mg), $K_2CO_3$ (1.5 mg), MeCN (0.45 mL), $H_2O$ (0.13 mL) |
| 2 | Azeotropic drying | $CH_3CN$ (1 mL), 110°C |
| 3 | Addition of precursor | 2.0 mg in DMSO (0.45 mL) |
| 4 | Fluorination | 110 °C, 10 min |
| 5 | Deprotection | aq. HCl (2.0 M, 0.2 mL), 110 °C, 3 min |
| 6 | Reaction quench | 0.2 M AcOK (4 mL) |
| 7 | Extraction of the product | Sep-PaktC18 Light, Washing ($H_2O$, 4 mL), Elution (70% EtOH, 0.7 mL) |
| 8 | Dilution of the eluate | With $H_2O$ (1.2 mL) |
| 9 | HPLC separation | Column: Inertsil ODS-4 (10 mm × 250 mm, particle size: 5 μm), Mobile phase: MeCN/20 mM NaH2PO4 (33/67), Flow rate: 5.0 mL/min, UV wavelength = 340 nm, Collection: Radioactive peak @ 20～21 min |
| 10 | Extraction of the product | (1) Fraction + $H_2O$(25 mL) + Ascorbic acid injection (25%, 1mL)<br>(2) Sep-Pak-tC18 → Washing ($H_2O$, 10 mL) → Elution (EtOH, 4 mL) |
| 11 | Formulation | (1) Eluate + Ascorbic acid injection* (25%, 0.2mL) + Polysorbate 80 (5% EtOH, 0.8 mL)<br>(2) Rotary evaporation (70°C, 4-5 min) → Saline (10 mL)<br>(3) Sterilization: Millex-GV Syringe Filter |

**Supplemental Table 2** Binding affinity of compounds against recombinant monoamine oxidase-B (MAO-B)

| Compound | Chemical structure | MAO-B ($IC_{50}$, nM) |
|---|---|---|
| **THK-5351** |  | 5.2 |
| **THK-5105** |  | 5.8 |
| **THK-5378** |  | 426.7 |
| **THK-5451** |  | 20.4 |
| **SMBT-0** |  | 60.6 |
| **SMBT-1** |  | 4.2 |
| **SMBT-2** |  | 555.0 |

| | | |
|---|---|---|
| **SMBT-3** |  | 294.0 |
| **SMBT-4** |  | 12.2 |
| **SMBT-5** |  | 12.9 |
| **Rasagiline** |  | 3.1 |
| **Lazabemide** |  | 1.9 |
| **Safinamide** |  | 1.4 |

**Supplemental Table 3: Inhibitory effects of SMBT-1 on radioligand binding to amyloid-β, tau, MAO-A, and MAO-B**

| Assay system | $IC_{50}$ (nM) | |
|---|---|---|
| | SMBT-1 | Positive substance |
| Amyloid-β (AD brain homogenate) | 1,000 | 2.2 (PiB) |
| Tau (AD brain homogenate) | 1,000 | 1.2 (MK-6240) |
| MAO-A (recombinant) | 713 | 2.6 (Fluoroethyl harmine) |
| MAO-B (recombinant) | 4.2 | 3.1 (Rasagiline) |

**Supplemental Table 4: Inhibitory effects of SMBT-1 on radioligand binding to various receptors, ion channels, and transporters**

| Assay system | Inhibition (%) | |
|---|---|---|
| | SMBT-1 | Positive substance |
| Adenosine A1 (Human) | 11.72 | 99.73 (DPCPX) |
| Adenosine A2a (Human) | 11.95 | 100.00 (CGS21680) |
| α1A-Adrenergic | 2.23 | 100.00 (Prazosin) |
| α1B-Adrenergic | 0.26 | 100.00 (Prazosin) |
| α2A-Adrenergic (Human) | 14.97 | 99.60 (Rauwolscine) |
| α2B-Adrenergic (Human) | 1.98 | 100.00 (Rauwolscine) |
| β1-Adrenergic (Human) | 0.00 | 100.00 ((±)-Propranolol) |
| β2-Adrenergic (Human) | 1.63 | 100.00 ((±)-Propranolol) |
| Androgen | 14.85 | 100.00 (Testosterone) |
| Angiotensin AT1 (Human) | 0.00 | 100.00 (Angiotensin II) |
| Bradykinin B1 (Human) | 0.00 | 100.00 (Lys-(des-Arg$^9$, Leu$^8$)-Bradykinin) |
| Bradykinin B2 (Human) | 3.30 | 97.85 (HOE140) |
| Ca channel (Type L, Benzothiazepine) | 2.79 | 100.00 ((+)-*cis*-Diltiazem) |
| Ca channel (Type L, Dihydropyridine) | 2.94 | 100.00 (Nitrendipine) |
| Ca channel (Type N) | 0.00 | 100.00 (ω-Conotoxin GVIA) |
| Dopamine D1 (Human) | 3.38 | 98.72 (R(+)-SCH-23390) |
| Dopamine D2 short (Human) | 8.18 | 99.64 ((+)-Butaclamol) |
| Dopamine D3 (Human) | 3.34 | 99.79 ((±)-7-OH-DPAT) |
| Dopamine D4.2 (Human) | 2.86 | 100.00 (Haloperidol) |
| Dopamine transporter (Human) | 37.94 | 100.00 (GBR12909) |
| Estrogen | 2.02 | 98.83 (β-Estradiol) |
| Endothelin ETA (Human) | 0.00 | 99.75 (Endothelin-1 human) |
| Endothelin ETB (Human) | 0.00 | 100.00 (Endothelin-1 human) |
| GABA A (Agonist site) | 2.05 | 97.50 (Muscimol) |
| GABA A (BZ central) | 0.02 | 99.96 (Diazepam) |
| GABA B | 5.95 | 99.94 (GABA) |

| | | |
|---|---|---|
| GABA transporter | 2.31 | 96.22 (GABA) |
| Glucocorticoid (Human) | 4.58 | 100.00 (Dexamethasone) |
| Glutamate (Kainate) | 0.00 | 99.72 (Kainic acid) |
| Glutamate (NMDA agonist site) | 0.00 | 99.77 (L-Glutamic acid) |
| Glutamate (NMDA glycine site) | 4.39 | 99.78 (MDL105,519) |
| Glutamate (NMDA phencyclidine site) | 0.20 | 99.92 ((+)-MK-801) |
| Histamine H1 (Human) | 12.18 | 100.00 (Pyrilamine) |
| Histamine H2 (Human) | 0.00 | 98.88 (Cimetidine) |
| Histamine H3 (Human) | 2.09 | 99.88 ((R)(−)-α-Methyl histamine) |
| Imidazoline (Central) | 6.15 | 100.00 (Guanabenz) |
| K channel KATP | 9.42 | 100.00 (Glybenclamide) |
| K channel SKCa | 0.50 | 99.92 (Apamin) |
| Leukotriene B4 | 2.92 | 100.00 (Leukotriene $B_4$) |
| Leukotriene D4 | 0.00 | 100.00 (Leukotriene $D_4$) |
| Muscarinic M1 (Human) | 6.12 | 99.74 (Atropine) |
| Muscarinic M2 (Human) | 0.84 | 99.84 (Atropine) |
| Muscarinic M3 (Human) | 0.00 | 99.98 (Atropine) |
| Na channel Site 2 | 6.84 | 100.00 (Dibucaine) |
| Neurokinin NK1 (Human) | 1.71 | 95.54 (L-703,606) |
| Neuropeptide Y1 (Human) | 0.00 | 99.33 (Neuropeptide Y human) |
| Neuropeptide Y2 (Human) | 5.15 | 100.00 (Neuropeptide Y human) |
| Norepinephrine transporter (Human) | 15.94 | 99.36 (Desipramine) |
| Nicotinic (Human) | 0.30 | 97.79 ((±)-Epibatidine) |
| Opiate δ (Human) | 15.10 | 99.51 (Naltriben) |
| Opiate κ (Human) | 6.11 | 99.41 (U-69593) |
| Opiate μ (Human) | 4.72 | 98.45 (DAMGO) |
| PAF | 5.14 | 99.80 (PAF) |
| Serotonin 5HT1A (Human) | 0.96 | 100.00 (Serotonin) |
| Serotonin 5HT2A (Human) | 2.49 | 99.90 (Ketanserin) |
| Serotonin 5HT3 (Human) | 6.65 | 99.43 (Tropisetron) |
| Serotonin transporter (Human) | 15.07 | 99.68 (Imipramine) |

| | | |
|---|---|---|
| Sigma σ1 | 4.70 | 100.00 ((+)-Pentazocine) |
| Sigma σ2 | 0.49 | 99.99 (Haloperidol) |
| Vasopressin V1 | 10.86 | 99.53 ([$Arg^8$]-Vasopressin) |

**Supplemental Table 5: Average absorbed dose estimates [μGy/MBq] for the target organs**

| Target Organs | SMBT-1 (male) | SMBT-1 (Female) |
|---|---|---|
| Adrenal | 12.2 | 15.2 |
| Brain | 4.13 | 5.27 |
| Breasts | 9.54 | 11.2 |
| Gallbladder wall | 16.7 | 21.2 |
| Lower large intestine wall | 34.5 | 45.9 |
| Small intestine | 80.8 | 114.0 |
| Stomach wall | 15.6 | 19.5 |
| Upper large intestine wall | 42.2 | 57.9 |
| Heart wall | 6.46 | 8.28 |
| Kidneys | 8.79 | 11.4 |
| Liver | 11.3 | 16.7 |
| Lungs | 6.09 | 7.81 |
| Muscle | 7.6 | 9.72 |
| Ovary | - | 28.4 |
| Pancreas | 13.7 | 16.7 |
| Red marrow | 12.4 | 14.8 |
| Osteogenic cells | 17.9 | 21.8 |
| Skin | 8.57 | 10.2 |
| Spleen | 6.87 | 8.9 |
| Testis | 11.0 | - |
| Thymus | 10.3 | 12.9 |
| Thyroid | 10.7 | 12.1 |
| Urinary bladder wall | 14.7 | 15.8 |
| Uterus | - | 25.7 |
| Total body | 12.2 | 15.6 |
| Effective dose [μSv/MBq] | **12.2** | **21.3** |