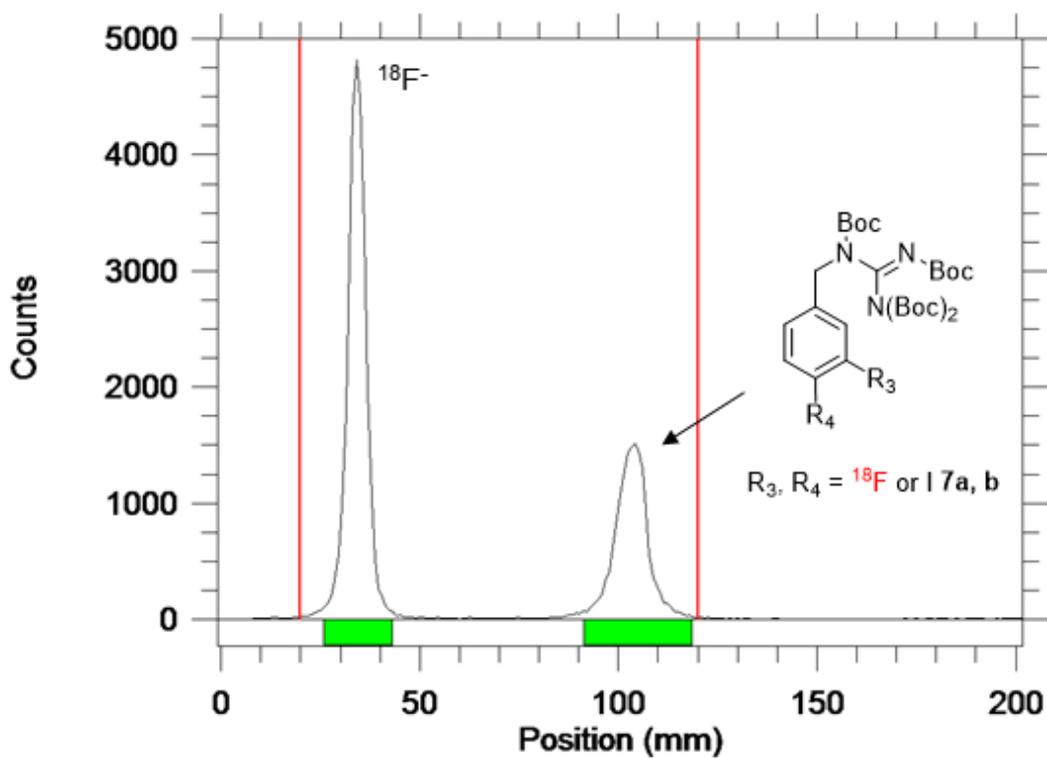
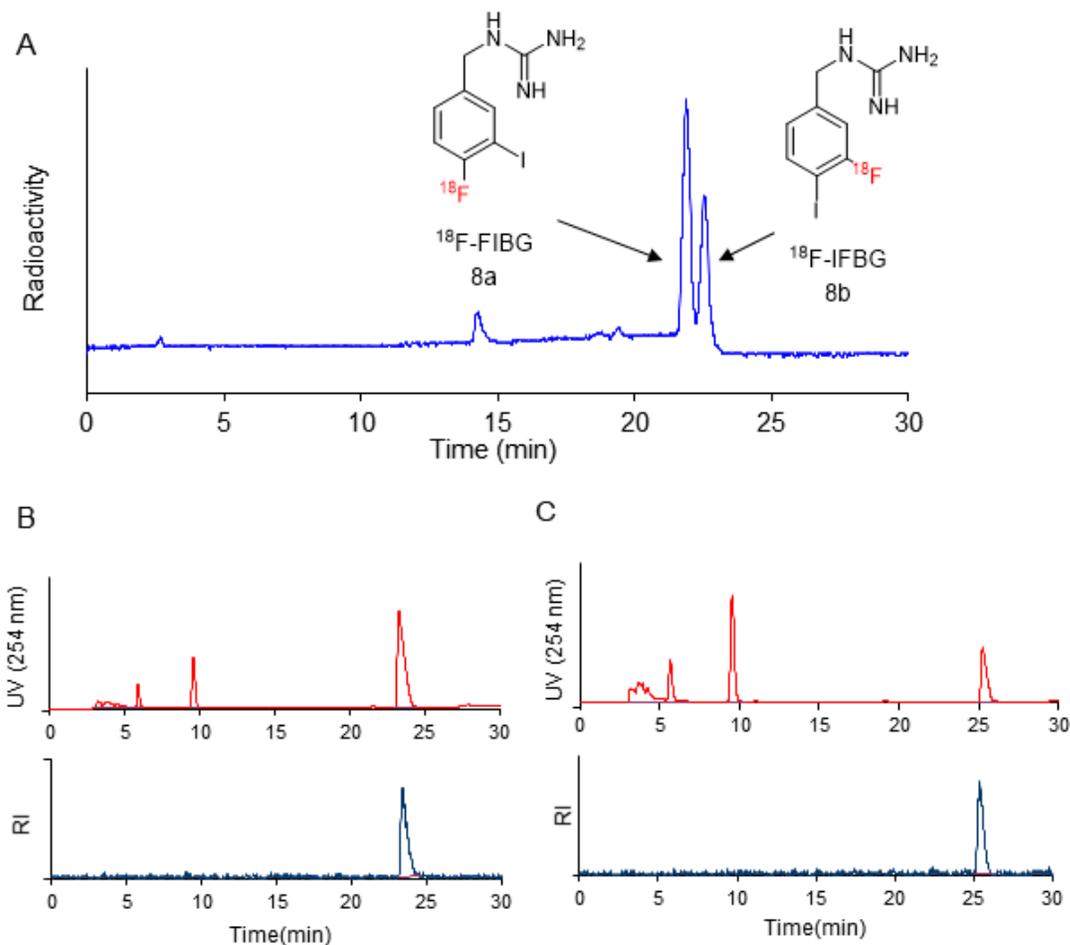


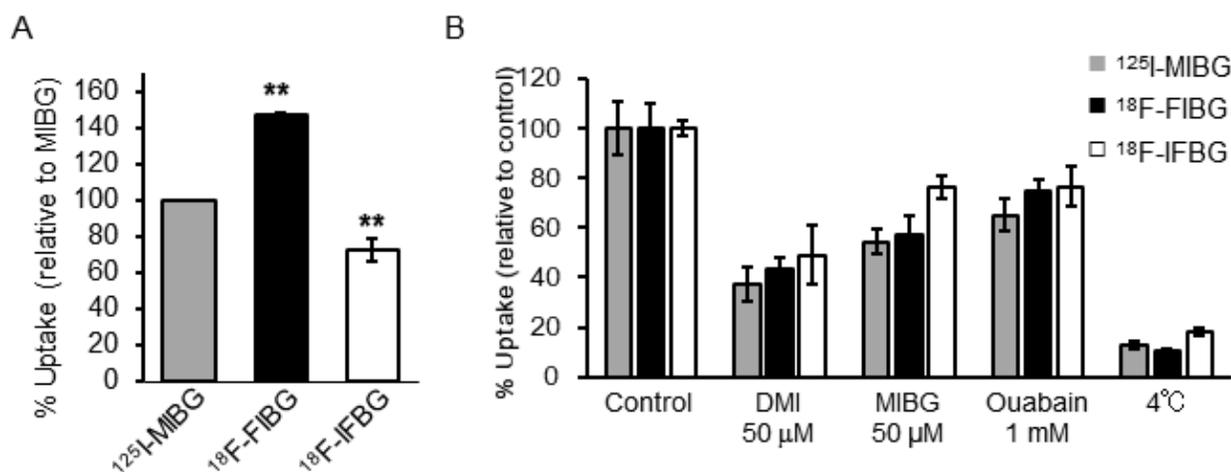
**Supplemental Figure 1.** Scheme and  $^{19}\text{F}$ -NMR data for cold- $^{19}\text{F}$ -fluorination. A, schematic image of the cold- $^{19}\text{F}$ -fluorination reaction. B,  $^{19}\text{F}$ -NMR spectrum (600 MHz,  $\text{CDCl}_3$ ) of the regioisomer mixture in the cold-fluorination reaction (upper panel), isomerically pure *tetra*-Boc-protected FIBG (middle panel), and IFBG (lower panel).  $^{19}\text{F}$ -NMR spectra are referenced based on the internal standard 1,3,5-trifluorobenzene ( $\delta -110.00$  ppm).



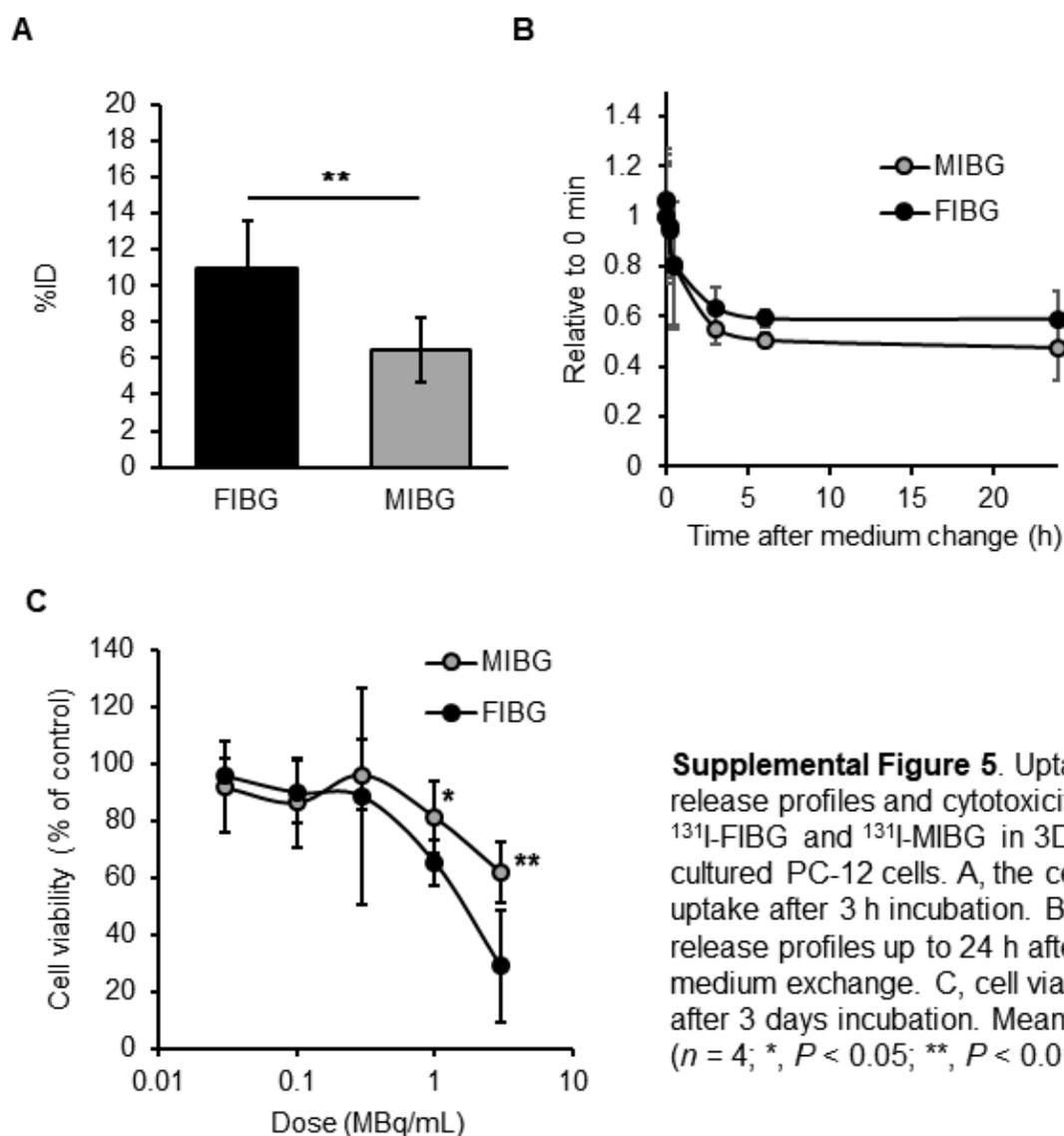
**Supplemental Figure 2.** Representative Radio-TLC results of the intermediate compound (**7a, b**). Eluent: hexane:ethyl acetate=1:1, R<sub>f</sub> = 0.16: unreacted  $^{18}\text{F}^-$ , R<sub>f</sub> = 0.8: **7a, b**



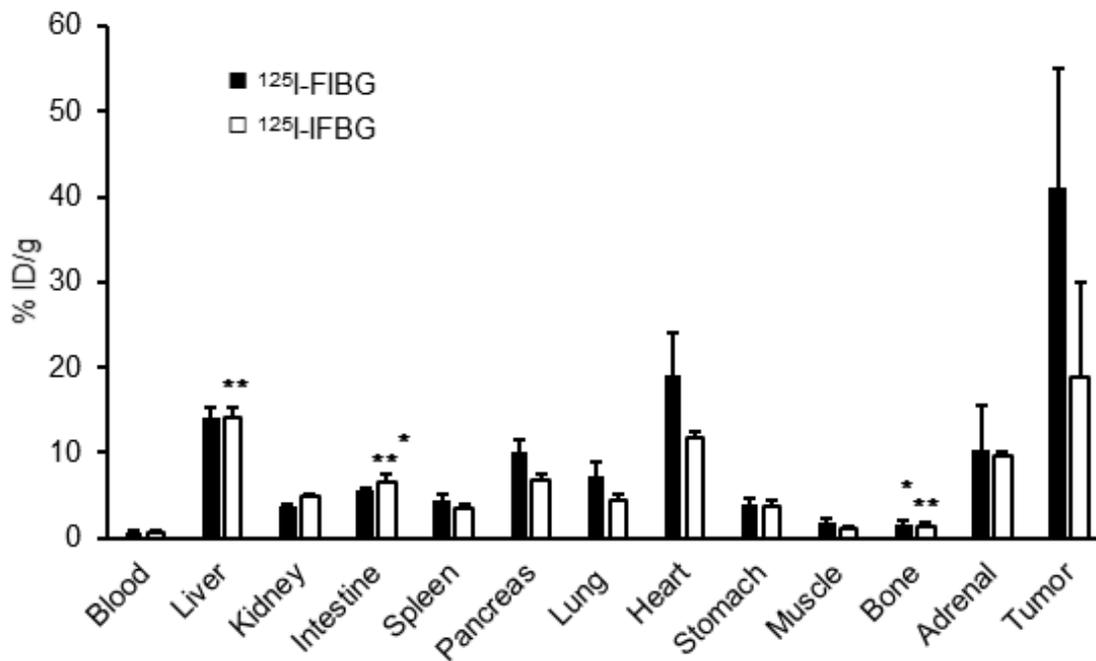
**Supplemental Figure 3.** HPLC profiles of  $^{18}\text{F}$ -FIBG and  $^{18}\text{F}$ -IFBG. A, semi-preparative HPLC. B and C, after purification spiked with cold standards.  $^{18}\text{F}$ -FIBG (8a) with FIBG (B),  $^{18}\text{F}$ -IFBG (8b) with IFBG (C). Semipreparative HPLC conditions: column COSMOSIL Cholester 10 mm I.D.  $\times$  250 mm; 5  $\mu\text{m}$  (Nacalai Tesque); flow rate 5 mL/min; eluents A = 0.1% TFA (v/v) in water and B = 0.1% TFA (v/v) in methanol; Gradient 0-30 min, 25-45% B; 30-35 min, 45-100% B; detection UV-vis 254 nm, RI ( $\gamma$  detector). Analytical HPLC were performed by using a COSMOSIL Cholester column of 4 mm I.D.  $\times$  250 mm, at a flow rate of 1 mL/min. Another conditions were the same with those of semipreparative HPLC.



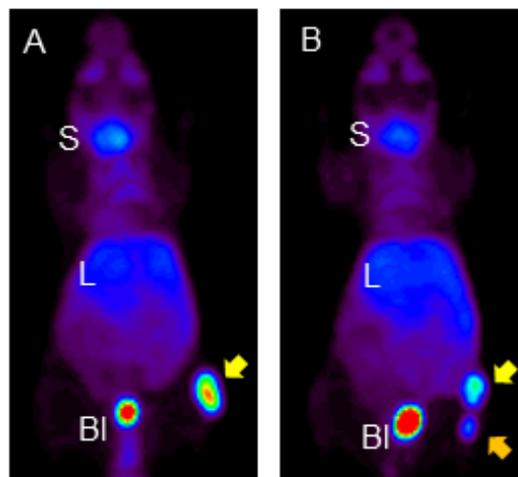
**Supplemental Figure 4.** A, relative uptake of  $^{18}\text{F}$ -FIBG or  $^{18}\text{F}$ -IFBG in PC-12 cells ( $n = 4$ ; \*\*,  $P < 0.01$ , paired  $t$ -test). B, effect of inhibitors on the uptake of MIBG analogs in PC-12 cells (mean  $\pm$  SD;  $n = 4$ ).



**Supplemental Figure 5.** Uptake, release profiles and cytotoxicity of  $^{131}\text{I}$ -FIBG and  $^{131}\text{I}$ -MIBG in 3D cultured PC-12 cells. A, the cellular uptake after 3 h incubation. B, release profiles up to 24 h after medium exchange. C, cell viability after 3 days incubation. Mean  $\pm$  SD ( $n = 4$ ; \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ )



**Supplemental Figure 6.** Biodistribution profiles of  $^{125}\text{I-FIBG}$  and  $^{125}\text{I-IFBG}$  in PC-12 xenograft mice at 1 h after injection. Mean  $\pm$  SD ( $n = 5$  per group; \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ , data are compared with each  $^{18}\text{F}$ -labeled counterpart by paired  $t$ -test)



**Supplemental Figure 7.** Representative 2 h PET images of  $^{18}\text{F-FIBG}$  and  $^{18}\text{F-IFBG}$  in PC-12 xenograft.  $^{18}\text{F-FIBG}$  (A) and  $^{18}\text{F-IFBG}$  (B). Arrows indicate tumor locations. S: Salivary gland, L: Liver, Bl: Bladder.

**Supplemental Table 1.** Biodistribution profiles of <sup>125</sup>I-FIBG and <sup>125</sup>I-MIBG in normal mice.

%ID/g	<sup>125</sup> I-FIBG							<sup>125</sup> I-MIBG						
	Time	10 m	1 h	3 h	6 h	1 day	3 days	7 days	10 m	1 h	3 h	6 h	1 day	3 days
Blood	0.81*	0.49	0.35	0.33	0.09	0.02	0.01	0.98	0.56	0.30	0.28	0.07	0.01	0.00
	0.09	0.11	0.10	0.09	0.02	0.01	0.00	0.13	0.11	0.05	0.03	0.01	0.01	0.00
Liver	7.33	8.89*	6.33*	4.69*	1.28*	0.46*	0.08*	6.62	7.19	2.98	2.35	0.48	0.09	0.03
	0.91	0.71	0.82	0.74	0.28	0.11	0.02	0.78	0.66	0.50	0.45	0.07	0.02	0.01
Kidney	7.40	2.29	1.34	1.38	0.51*	0.25	0.04	4.73	2.76	1.18	1.57	0.16	0.07	0.01
	2.33	0.32	0.30	0.13	0.11	0.11	0.03	0.72	0.55	0.22	1.19	0.07	0.02	0.01
Intestine	3.25	2.95	3.21	2.37	1.13*	0.41*	0.06*	3.97	3.63	2.43	2.74	0.65	0.11	0.02
	0.77	0.32	0.48	0.31	0.29	0.11	0.03	0.25	0.71	0.47	0.24	0.11	0.02	0.01
Spleen	3.85	2.36	1.78	2.03	1.38*	0.77*	0.06	3.52	2.13	1.50	1.55	0.31	0.04	0.01
	0.68	0.61	0.24	0.29	0.33	0.21	0.03	0.24	0.20	0.40	0.59	0.23	0.02	0.01
Pancreas	11.0*	6.74	3.90	3.95	1.19	0.43*	0.05*	9.29	6.53	2.69	2.19	0.41	0.07	0.00
	1.39	0.40	1.30	0.53	0.52	0.12	0.03	0.98	0.90	0.48	0.37	0.03	0.01	0.01
Lung	14.3	6.04	3.53	2.70	1.27*	0.35*	0.05	12.6	4.81	2.90	2.42	0.43	0.06	0.03
	1.24	1.27	0.52	0.16	0.20	0.09	0.03	3.06	0.33	0.50	0.32	0.16	0.01	0.03
Heart	11.5	10.4	9.62*	8.71*	6.09*	1.99*	0.23*	13.12	9.47	6.08	5.51	1.07	0.13	0.02
	1.01	1.58	1.33	1.29*	1.12	0.34	0.13	1.98	0.47	0.76	1.05	0.20	0.05	0.01
Stomach	2.32	2.11	1.18	1.22	0.57	0.27*	0.08	2.38	2.18	1.22	1.88	0.52	0.18	0.06
	0.73	0.16	0.39	0.25	0.12	0.02	0.05	0.57	0.67	0.25	0.24	0.03	0.04	0.01
Muscle	1.73	1.32	1.10	1.00	0.39*	0.15*	0.09	1.52	1.50	0.87	0.92	0.16	0.03	0.00
	0.57	0.17	0.37	0.25	0.13	0.05	0.16	0.56	0.34	0.18	0.15	0.05	0.02	0.00
Bone	1.92	1.49	1.76*	1.41	0.54	0.10	0.01	2.13	1.82	1.13	1.16	0.24	0.05	0.00
	0.20	0.59	0.16	0.43	0.22	0.05	0.01	0.64	0.25	0.22	0.46	0.08	0.04	0.01
Adrenal	12.9	11.3	11.3	9.37	17.4*	16.4*	10.2	12.7	9.24	5.92	15.2	13.3	8.46	7.39
	3.37	4.83	2.87	4.79	2.87	3.52	3.51	5.07	6.53	4.02	4.50	1.46	3.19	1.55

Data represent %ID/g (upper row: averaged, lower row: SD). \* statistically significant ( $P < 0.05$ ).

**Supplemental Table 2.** Biodistribution profiles of  $^{131}\text{I}$ -FIBG and  $^{125}\text{I}$ -MIBG in PC-12 tumor-bearing mice.

	FIBG						MIBG					
	1 h	3 h	6 h	24 h	48 h	5 days	1 h	3 h	6 h	24 h	48 h	5 days
Blood	1.50	0.94 <sup>†</sup>	0.55	0.13	0.07 <sup>†</sup>	0.03 <sup>†</sup>	2.51	1.01	0.70	0.10	0.08	0.02
	0.36	0.08	0.06	0.03	0.03	0.00	1.17	0.11	0.07	0.02	0.06	0.02
Liver	15.8	12.2	7.96	2.24	1.51	0.45	10.0	5.67	3.32	0.52	0.24	0.04
	2.26	0.11	0.58	0.22	0.28	0.04	1.48	0.25	0.39	0.07	0.03	0.01
Kidney	4.16	2.61	2.45	1.01	0.58	0.20	3.31	1.75	1.49	0.28	0.13	0.05
	0.25	0.17	0.25	0.11	0.13	0.03	0.41	0.20	0.25	0.05	0.02	0.02
Intestine	7.42	6.75 <sup>†</sup>	6.10	2.18	1.55	0.45	6.65	6.94	5.63	1.06	0.45	0.09
	0.94	0.41	0.61	0.17	0.37	0.05	0.86	0.50	0.65	0.06	0.10	0.03
Spleen	5.79	5.57	4.68	4.07	2.39	0.91	4.42	4.10	2.79	1.30	0.44	0.10
	0.40	0.46	0.48	0.36	0.73	0.16	0.62	0.26	0.17	0.18	0.18	0.04
Pancreas	10.2	7.83	6.92	2.40	1.45	0.32	6.80	3.87	2.63	0.54	0.18	0.01
	1.14	0.68	0.81	0.39	0.36	0.09	0.89	0.38	0.42	0.13	0.04	0.01
Lung	11.6	6.92	6.44	2.02	1.11	0.33	6.71	3.47	3.01	0.48	0.18	0.07
	1.94	2.15	0.75	0.17	0.25	0.03	1.02	0.85	0.62	0.09	0.07	0.02
Heart	18.9	16.81	17.55	9.87	5.19	1.25	13.2	9.40	7.58	1.79	0.56	0.10
	2.73	2.09	0.93	1.10	1.36	0.46	2.82	1.18	0.52	0.34	0.14	0.02
Stomach	6.94	5.74	4.35	1.63 <sup>†</sup>	1.38	0.77	11.0	8.44	5.26	1.07	0.68	0.24
	0.78	0.74	0.42	0.67	0.51	0.15	2.20	2.75	0.38	0.42	0.27	0.07
Muscle	1.57	1.31	1.02	0.47	0.26	0.03 <sup>†</sup>	1.22	0.80	0.78	0.20	0.08	0.02
	0.29	0.41	0.10	0.11	0.18	0.05	0.27	0.23	0.26	0.05	0.06	0.03
Adrenal	11.8	8.52 <sup>†</sup>	9.38 <sup>†</sup>	9.47	9.06	5.87	8.96	6.84	7.90	5.71	5.13	1.86
	3.73	3.47	2.22	2.32	3.17	0.65	4.04	1.65	2.48	1.10	1.70	2.13
Tumor	61.2	77.0	73.4	83.9	49.0	18.4	50.1	59.0	54.9	39.6	10.7	1.46
	10.6	9.38	5.30	7.37	5.67	3.78	9.38	9.18	5.62	7.14	2.76	0.36

Data represent %ID/g (upper row: averaged, lower row: SD). <sup>†</sup> statistically **not** significant by paired t-test ( $P > 0.05$ ).

**Supplemental Table 3.** Days required for a 2.5-fold increase in volume of PC-12 tumor

Treatment	Days	<i>P</i> -value	
	Average (SD)	vs. control	vs. MIBG
Control	8.00 (3.08)		
MIBG 10 MBq	22.6 (2.88)	0.0003	
FIBG 10 MBq	31.7 (2.88)	< 0.0001	0.033
FIBG 5 MBq	29.8 (3.89)	< 0.0001	n.s.
FIBG 3 MBq	28.8 (5.22)	< 0.0001	n.s.
FIBG 1 MBq	15.7 (10.3)	n.s.	n.s.