

Supplementary data

GRPR-antagonists carrying DOTAGA-chelator via positively-charged linkers: Perspectives for prostate cancer theranostics

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Table S1. Biodistribution data (%IA/g \pm sd, n= 4) of [¹¹¹In]In-AU-RM26-M1, [¹¹¹In]In-AU-RM26-M2, [¹¹¹In]In-AU-RM26-M3, and [¹¹¹In]In-AU-RM26-M4 in PC-3 xenografted mice; at 4 h pi for [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M3 and at 4 h and 24 h pi for [¹¹¹In]In-AU-RM26-M2 and [¹¹¹In]In-AU-RM26-M4; results during in vivo GRPR-blockade by coinjection of excess NOTA-PEG2-RM26 at 4 h pi for [¹¹¹In]In-AU-RM26-M2 and [¹¹¹In]In-AU-RM26-M4 are also included (Block, values shown in italics; n= 3). Uptake in GIT and carcass is given as %IA \pm sd (n= 4).

Organ	M1	M2		M3	M4	
	4 h	4 h	24 h	4 h	4 h	24 h
Blood	0.04 \pm 0.01	0.003 \pm 0.002 <i>0.06 \pm 0.01</i>	0.01 \pm 0.002	0.024 \pm 0.002	0.122 \pm 0.0013 <i>0.08 \pm 0.01</i>	0.02 \pm 0.01
Lungs	0.08 \pm 0.05	0.05 \pm 0.01 <i>0.07 \pm 0.01</i>	0.05 \pm 0.02	0.12 \pm 0.01	0.2 \pm 0.08 <i>0.10 \pm 0.0002</i>	0.06 \pm 0.02
Liver	0.2 \pm 0.1	0.12 \pm 0.01 <i>0.15 \pm 0.01</i>	0.11 \pm 0.01	0.17 \pm 0.01	0.6 \pm 0.11 <i>0.45 \pm 0.11</i>	0.31 \pm 0.07
Spleen	0.08 \pm 0.02	0.07 \pm 0.02 <i>0.07 \pm 0.01</i>	0.07 \pm 0.01	0.08 \pm 0.01	0.23 \pm 0.07 <i>0.12 \pm 0.004</i>	0.14 \pm 0.04
Pancreas	0.2 \pm 0.1	0.37 \pm 0.08 ^e <i>0.05 \pm 0.01</i>	0.15 \pm 0.03	0.06 \pm 0.01 ^f	3.4 \pm 0.6 ^{e,f,h} <i>0.20 \pm 0.05ⁱ</i>	0.36 \pm 0.08 ^{h,j}
Small Int	0.10 \pm 0.04	0.10 \pm 0.06 <i>0.06 \pm 0.02</i>	0.06 \pm 0.03	0.08 \pm 0.03	1.1 \pm 0.3 <i>0.13 \pm 0.04</i>	0.11 \pm 0.03
Kidneys	6.4 \pm 0.6 ^{b,g}	5 \pm 1 <i>5.7 \pm 0.3</i>	4.1 \pm 0.4	3.4 \pm 0.2 ^{b,f}	7 \pm 1 ^{g,f,h} <i>6 \pm 1</i>	2.7 \pm 0.1 ^h
Tumor	6 \pm 2 ^{b,c}	7 \pm 2 ^{d,e,g,j} <i>0.9 \pm 0.4ⁱ</i>	4.9 \pm 0.7 ^{g,k}	2.5 \pm 0.6 ^{b,d,f}	15 \pm 5 ^{c,e,f,h,j} <i>1.4 \pm 0.6^j</i>	7 \pm 3 ^{h,k}
Muscle	0.04 \pm 0.02	0.02 \pm 0.01 <i>0.02 \pm 0.003</i>	0.02 \pm 0.01	0.03 \pm 0.01	0.06 \pm 0.02 <i>0.05 \pm 0.02</i>	0.02 \pm 0.01
Bone	0.05 \pm 0.01	0.05 \pm 0.03 <i>0.05 \pm 0.01</i>	0.04 \pm 0.02	0.06 \pm 0.01	0.13 \pm 0.04 <i>0.08 \pm 0.004</i>	0.09 \pm 0.02
GI	0.9 \pm 0.1	0.8 \pm 0.5 <i>0.46 \pm 0.03</i>	0.13 \pm 0.03	1.3 \pm 0.9	1.4 \pm 0.3 <i>0.5 \pm 0.2</i>	0.15 \pm 0.03
Carcass	1.3 \pm 0.5	0.8 \pm 0.1 ^e <i>1 \pm 0.5</i>	0.5 \pm 0.2	1.7 \pm 0.3	3 \pm 1.5 ^{e,h} <i>1.6 \pm 0.3</i>	0.8 \pm 0.2 ^h

^{a-k} Two-way Anova with Tuckey's post hoc analysis ($p < 0.05$): ^a Significant difference between [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M2; ^b Significant difference between [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M3; ^c Significant difference between [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M4; ^d Significant difference between [¹¹¹In]In-AU-RM26-M2 and [¹¹¹In]In-AU-RM26-M3; ^e Significant difference between [¹¹¹In]In-AU-RM26-M2 and [¹¹¹In]In-AU-RM26-M4 at 4 h pi; ^f Significant difference between [¹¹¹In]In-AU-RM26-M3 and [¹¹¹In]In-AU-RM26-M4; ^g Significant difference between [¹¹¹In]In-AU-RM26-M2 at 4 and 24 h pi; ^h Significant difference between [¹¹¹In]In-AU-RM26-M4 at 4 and 24 h pi; ⁱ Significant difference between [¹¹¹In]In-AU-RM26-M2 4 h and block; ^j Significant difference between [¹¹¹In]In-AU-RM26-M4 4 h and block; ^k Significant difference between [¹¹¹In]In-AU-RM26-M3 and [¹¹¹In]In-AU-RM26-M4 at 24 h pi; unless clearly stated, differences refer to values at 4 h pi.

Table S2. Tumor-to-organ ratios of [¹¹¹In]In-AU-RM26-M1 (M1), [¹¹¹In]In-AU-RM26-M2 (M2), [¹¹¹In]In-AU-RM26-M3 (M3) and [¹¹¹In]In-AU-RM26-M4 (M4) in PC-3 tumor-bearing mice; for [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M3 at 4 h pi and for [¹¹¹In]In-AU-RM26-M2 and [¹¹¹In]In-AU-RM26-M4 at 4 h and 24 h pi.

Organ	M1	M2		M3	M4	
	4 h	4 h	24 h	4 h	4 h	24 h
Blood	133 ± 26	265 ± 99 ^{c,d,e}	471 ± 60 ^c	104 ^d ± 29	123 ± 43 ^{e,g}	369 ± 228 ^g
Lungs	81 ± 25	173 ± 50	101 ± 37	33 ± 22	90 ± 59	120 ± 61
Liver	39 ± 5	60 ± 16	43 ± 3	15 ± 4.5	25 ± 11	23 ± 9
Spleen	72 ± 9.5	109 ± 15	74 ± 20	31 ± 9	71 ± 37	54 ± 30
Pancreas	27 ± 4	19 ± 2	32 ± 3	45 ± 15	4 ± 1	20 ± 5
Small Int	57 ± 7	70 ± 42	87 ± 33	35 ± 15	15 ± 7	67 ± 35
Kidneys	0.9 ± 0.2	1.6 ± 0.7	1.20 ± 0.15	0.7 ± 0.2	2.3 ± 0.9	2.6 ± 0.9
Muscle	234 ± 154 ^{a,b}	478 ± 298 ^{a,c,d,e}	313 ± 127 ^c	75 ± 18 ^{b,d,f}	307 ± 168 ^{e,f}	347 ± 176
Bone	117 ± 16	184 ± 156	157 ± 91	39 ± 8	119 ± 40	79 ± 25

Two-way Anova with Tuckey's post hoc analysis ($p < 0.05$): ^a Significant difference between [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M2 (4 h pi); ^b Significant difference between [¹¹¹In]In-AU-RM26-M1 and [¹¹¹In]In-AU-RM26-M3 (4 h pi); ^c Significant difference between [¹¹¹In]In-AU-RM26-M2 4 h and 24 h pi; ^d Significant difference between [¹¹¹In]In-AU-RM26-M2 (4 h pi) and [¹¹¹In]In-AU-RM26-M3 (4 h pi); ^e Significant difference between [¹¹¹In]In-AU-RM26-M2 (4 h pi) and [¹¹¹In]In-AU-RM26-M4 (4 h pi); ^f Significant difference between [¹¹¹In]In-AU-RM26-M3 and [¹¹¹In]In-AU-RM26-M4 (4 h pi); ^g Significant difference between [¹¹¹In]In-AU-RM26-M4 4 h pi and 24 h pi.