



Supplemental Materials

Optimizing the Profile of [^{99m}Tc]Tc-NT(7–13) Tracers in Pancreatic Cancer Models by Means of Protease Inhibitors

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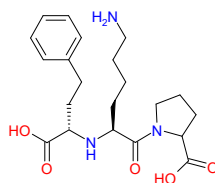
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(a)



(b)

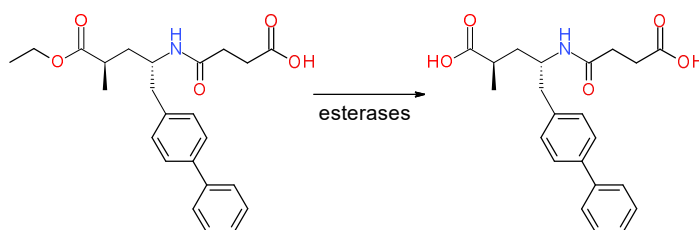


Figure S1. Structure of (a) the angiotensin converting enzyme (ACE)-inhibitor lisinopril (Lis) and (b) the structure of sacubitril (AHU377) found in the drug Entresto, releasing the active substance sacubitrilat (LBQ657) in vivo upon ester-hydrolysis by esterases; sacubitrilat is a potent and specific inhibitor of neprilysin (NEP).

Table S1. Cellular uptake (membrane bound and internalized of total-added activity) of [^{99m}Tc]Tc-DT1 at 1 h incubation across cell lines, expressed as mean \pm SD, including specific and non-specific portions.

Cell line		MB ¹	I ²
AsPC-1	specific	0.98 \pm 0.42	14.11 \pm 2.28
	non-specific ³	0.67 \pm 0.23	0.88 \pm 0.59
PANC-1	specific	0.76 \pm 0.39	7.30 \pm 2.41
	non-specific	0.44 \pm 0.20	0.29 \pm 0.12
MiaPaca-2	specific	0.37 \pm 0.23	2.46 \pm 0.23
	non-specific	0.87 \pm 0.49	0.50 \pm 0.36
Capan-1	specific	0.10 \pm 0.01	0.28 \pm 0.13
	non-specific	0.20 \pm 0.02	0.11 \pm 0.02

¹ MB, membrane bound fraction; ² I, internalized fraction; non-specific values determined by incubation in the presence of 1 μM NT; these values were subtracted from the respective measured MB/I fractions to calculate the respective specific values.

Table S2. Biodistribution data for [^{99m}Tc]Tc-DT1, expressed as %IA/g mean \pm SD, in MiaPaca-2 xenograft-bearing SCID mice treated with the Entresto+Lis combination at 4 h pi.

Tissue	[^{99m}Tc]Tc-DT1 – 4 h pi
	Entresto+Lis ²
Blood	0.06 \pm 0.01
Liver	0.57 \pm 0.04
Heart	0.08 \pm 0.02
Kidneys	5.86 \pm 0.14
Stomach	0.37 \pm 0.05
Intestines	2.43 \pm 0.6
Spleen	0.49 \pm 0.03
Muscle	0.03 \pm 0.01
Lungs	0.43 \pm 0.04
Pancreas	0.1 \pm 0.02
Tumor	1.97 \pm 0.25

All animals were injected with 185 kBq/10 pmol peptide; Entresto+Lis mice group (n = 4) with animals receiving 12 mg Entresto per os 30 min prior to radiotracer co-injection together with 200 μg Lis to in situ inhibit NEP and ACE, respectively.