Supporting Information

Drug Conjugation Affects Pharmacokinetics and Specificity of Kidney-Targeted Peptide Carriers

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Table of contents

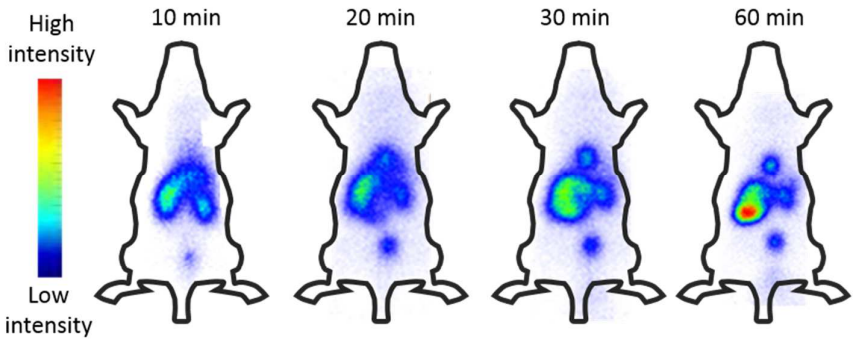

Figure S1: Time course of the scintigraphic distribution of LA-^{125}I-y(MARIA)$_3$ after bolus injection in NMRI mouse. The conjugate shows a changed pharmacokinetic in comparison to bare peptide ^{125}I-y(MARIA)$_3$. Changed excretion route over bile and liver can be assumed (**Error! Reference source not found.~~Figure S2~~**).

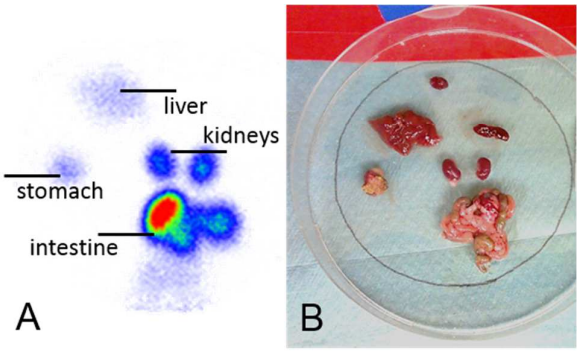

Figure S2: Scintigraphic imaging of organs 60 min after bolus injection of LA-^{125}I-y(MARIA)$_3$ in NMRI mouse. **(A)** Majority of detected radiation was found in intestine, which indicates a changed excretion route of the peptide via bile into liver and intestine. Less amounts are detected in kidneys, liver and stomach. **(B)** Corresponding organs.

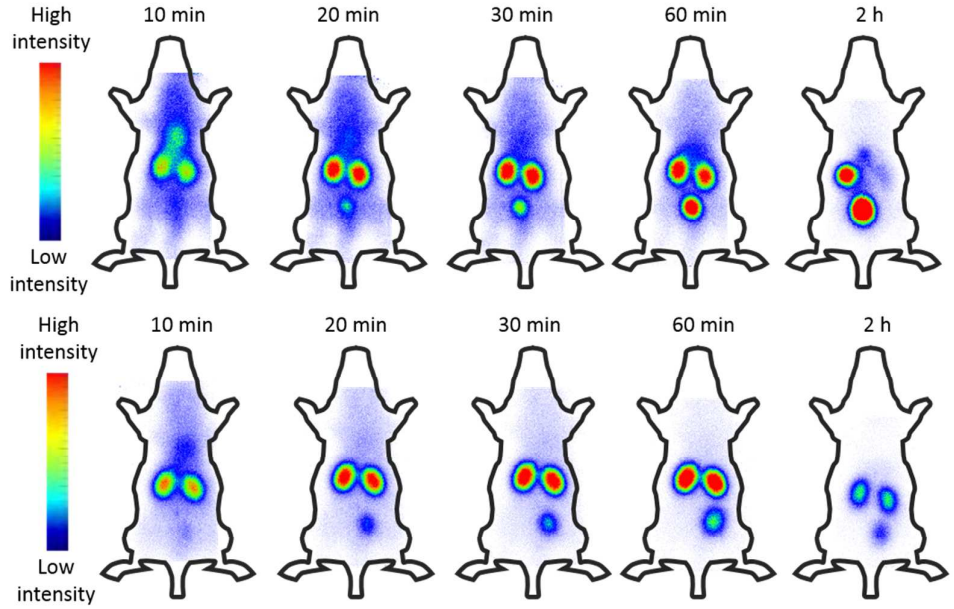

Figure S3: Time course of the scintigraphic distribution of $(KKEEE)_3K$ after conjugation with the hydrophilic caffeic acid *N*-terminally versus double ε-binding after bolus injection in NMRI mouse. **Upper row:** *N*-terminally conjugated, caffeic acid-^{125}I-y$(KKEEE)_3K$. **Bottom row:** ε-bounded, ^{125}I-y (KKK(ε-caffeic acid)$(EEEKK)_2$K(ε-caffeic acid) showed a higher specificity in comparison to *N*-terminally bounded caffeic acid conjugate, even after double loading.

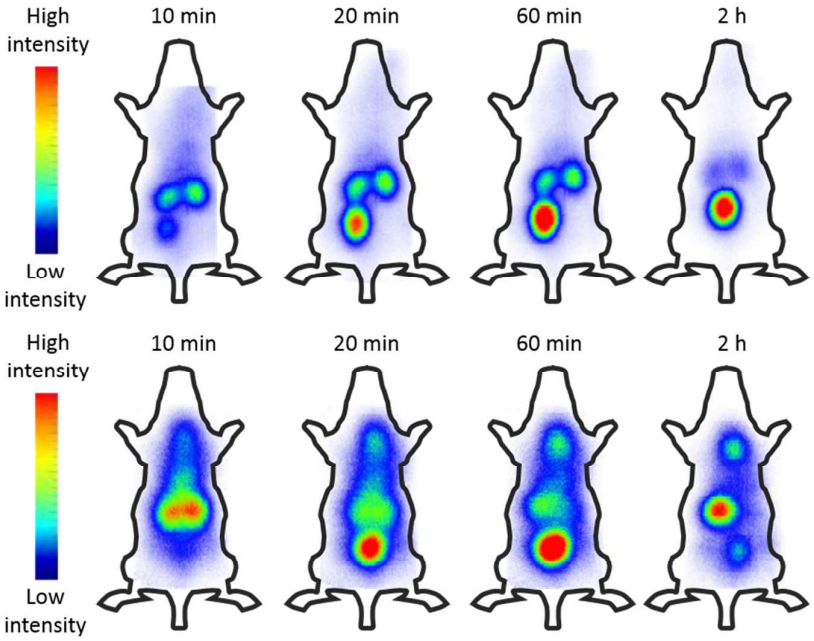

Figure S4: D-tyrosine versus L-tyrosine radiolabeling. **Upper Row:** The radiolabeling of $(K\varepsilon)_{10}$y-^{125}I via a D-tyrosine results in a tracer with stable accumulation in the kidneys followed by excretion to the bladder. **Bottom row:** In contrast, scintigraphic distribution of $(K\varepsilon)_{10}$Y-^{125}I via radiolabeling of a naturally L-tyrosine leads to distribution in upper body followed by accumulation in stomach and thyroid. This indicates the deiodation of the peptide tracer.

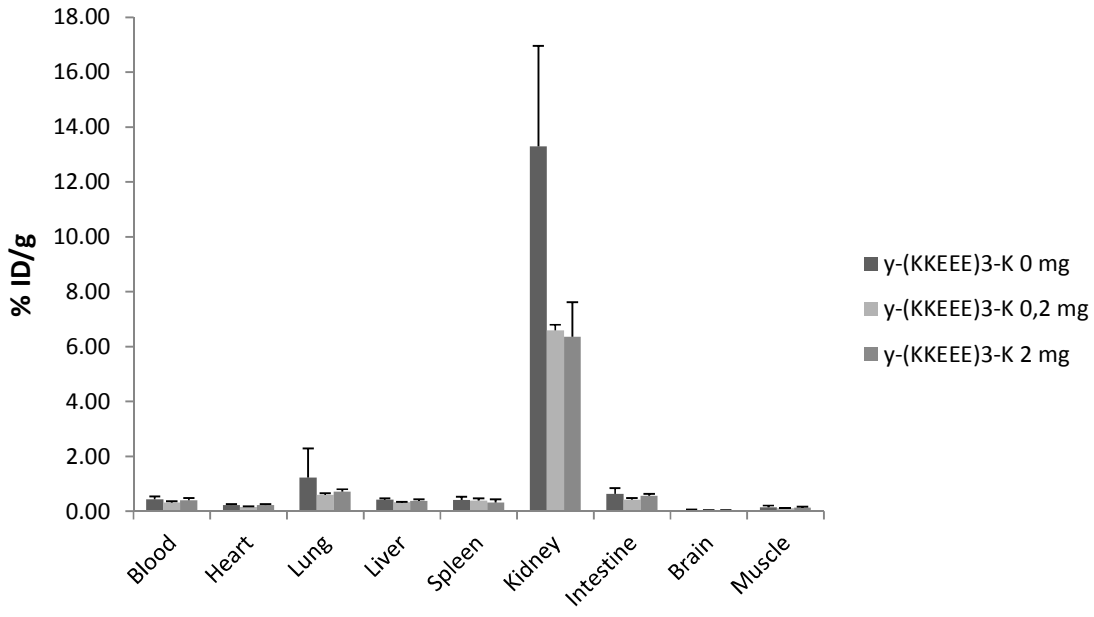

Figure S5: Competitive ligand-receptor study of two different peptides. Figure shows biodistribution study of ^{177}Lu-DOTATOC, 60 minutes after application into three female NMRI-mice per group. The simultaneous application of the peptide y$(KKEEE)_3$K lead to a decrease of the renal accumulation of ^{177}Lu-DOTATOC by ~50%.