Effect of Peptide Length on *in Vitro* and *in Vivo* Properties of 177Lu-labeled Peptide Analogs Targeting CCK2R

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# **Figure S1.** UV-chromatogram of (a) DOTA-MGS5, (b) **1** and (c) **2**



# **Figure S2**. Mass spectra of (a) DOTA-MGS5, (b) **1** and (c) **2**

# **Table S1.** Results of biodistribution studies evaluated in A431-CCK2R/A431-mock xenografted BALB/c nude mice of the 177Lu-labeled peptide derivatives (20 pmol, 4 h p.i.)

|  |  |  |  |
| --- | --- | --- | --- |
| radiopeptide | [177Lu]Lu-DOTA-MGS5 | [177Lu]Lu-1 | [177Lu]Lu-2  % |
| blood | 0.11 ± 0.11 | 0.02 ± 0.00 | 0.03 ± 0.01 |
| lung | 0.17 ± 0.14 | 0.12 ± 0.04 | 0.22 ± 0.06 |
| heart | 0.10 ± 0.06 | 0.06 ± 0.01 | 0.07 ± 0.02 |
| femur | 0.36 ± 0.35 | 0.21 ± 0.05 | 0.22 ± 0.15 |
| muscle | 0.10 ± 0.02 | 0.04 ± 0.02 | 0.06 ± 0.03 |
| spleen | 0.27 ± 0.18 | 1.86 ± 0.62 | 0.96 ± 0.30 |
| intestine | 1.02 + 0.23 | 0.42 ± 0.07 | 0.60 ± 0.12 |
| liver | 1.02 ± 0.80 | 2.48 ± 0.39 | 1.43 ± 0.18 |
| kidneys | 3.45 ± 0.91 | 21.60 ± 2.11 | 1.96 ± 0.29 |
| stomach | 6.26 + 4.28 | 4.77 ± 1.10 | 4.30 ± 0.95 |
| pancreas | 1.91 + 0.91 | 1.25 ± 0.27 | 0.72 ± 0.14 |
| A431-CCK2R | 22.89 ± 4.67 | 22.18 ± 6.23 | 32.10 ± 4.05 |
| A431-mock | 0.19 ± 0.03 | 0.14 + 0.04 | 0.22 + 0.06 |

# **Table S2.** Results of the blocking experiments using 1000-fold excess of non-radiolabeled peptide in the biodistribution studiy evaluated in A431-CCK2R/A431-mock xenografted BALB/c nude mice of the 177Lu-labeled peptide derivatives (20 pmol, 4 h p.i.)

|  |  |  |  |
| --- | --- | --- | --- |
| radiopeptide | [177Lu]Lu-DOTA-MGS5 | [177Lu]Lu-1 | [177Lu]Lu-2  % |
| blood | 0.09 | 0.03 | 0.02 |
| lung | 0.08 | 0.06 | 0.20 |
| heart | 0.08 | 0.05 | 0.04 |
| femur | 0.04 | 0.18 | 0.09 |
| muscle | 0.03 | 0.02 | 0.04 |
| spleen | 0.16 | 1.13 | 0.70 |
| intestine | 0.79 | 0.17 | 0.45 |
| liver | 0.54 | 2.86 | 1.13 |
| kidneys | 2.95 | 9.21 | 1.47 |
| stomach | 0.09 | 0.06 | 0.09 |
| pancreas | 0.11 | 0.05 | 0.05 |
| A431-CCK2R | 0.54 | 0.45 | 0.39 |
| A431-mock | 0.34 | 0.12 | 0.16 |



# **Figure S3.** Uptake of [177Lu]Lu-**2** in the residual organs of A431-CCK2 xenografted BALB/c nude mice for up to 7 days.

# **Table S3**. Uptake values of [177Lu]Lu-**2** in A431-CCK2R tumor xenograft for up to 7 days.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Timepoint p.i. | 1 h  [% IA/g] | 24 h  [% IA/g] | 3 days  [% IA/g] | 7 days  [% IA/g] |
| blood | 1.45±0.30 | 0.01±0.00 | 0.00±0.00 | 0.01±0.00 |
| lung | 4.33±0.87 | 0.09±0.02 | 0.06±0.01 | 0.02±0.01 |
| heart | 0.62±0.12 | 0.05±0.01 | 0.02±0.00 | 0.02±0.00 |
| femur | 0.23±0.05 | 0.05±0.01 | 0.03±0.01 | 0.04±0.02 |
| muscle | 0.22±0.05 | 0.03±0.00 | 0.01±0.00 | 0.01±0.01 |
| spleen | 0.54±0.08 | 0.19±0.03 | 0.13±0.02 | 0.09±0.04 |
| intestine | 1.00±0.34 | 0.16±0.02 | 0.08±0.00 | 0.03±0.00 |
| liver | 0.95±0.12 | 0.38±0.08 | 0.18±0.01 | 0.06±0.01 |
| kidneys | 2.84±0.42 | 1.32±0.23 | 0.72±0.10 | 0.31±0.03 |
| stomach | 5.43±1.05 | 3.66±0.38 | 2.28±0.33 | 0.88±0.12 |
| pancreas | 0.85±0.14 | 0.41±0.08 | 0.28±0.04 | 0.16±0.04 |
| A431-CCK2R tumor | 56.29±9.14 | 33.61±2.95 | 12.52±0.96 | 1.23±0.53 |