Interdyscyplinarne **Studia Doktoranckie**
RadFarm – Radiofarmaceutyki dla ukierunkowanej molekularnie diagnostyki i terapii medycznej

radfarm@ncbj.gov.pl, www.ncbj.gov.pl/radfram

Preparation of targeted radiopharmaceuticals based on NK-1 receptor antagonists for diagnosis and therapy of oncological pathologies

MPharm. Paweł Krzysztof Halik

Scientific supervisor: Dr hab. Ewa Gniazdowska, prof. ICHTJ (ICHTJ)
Additional supervisor: Prof. dr hab. n. farm. Grażyna Nowicka (WUM)

Centre of Radiochemistry and Nuclear Chemistry,
Institute of Nuclear Chemistry and Technology

Fundusze Europejskie Wiedza Edukacja Rozwój
Rzeczpospolita Polska
Unia Europejska Europejski Fundusz Społeczny

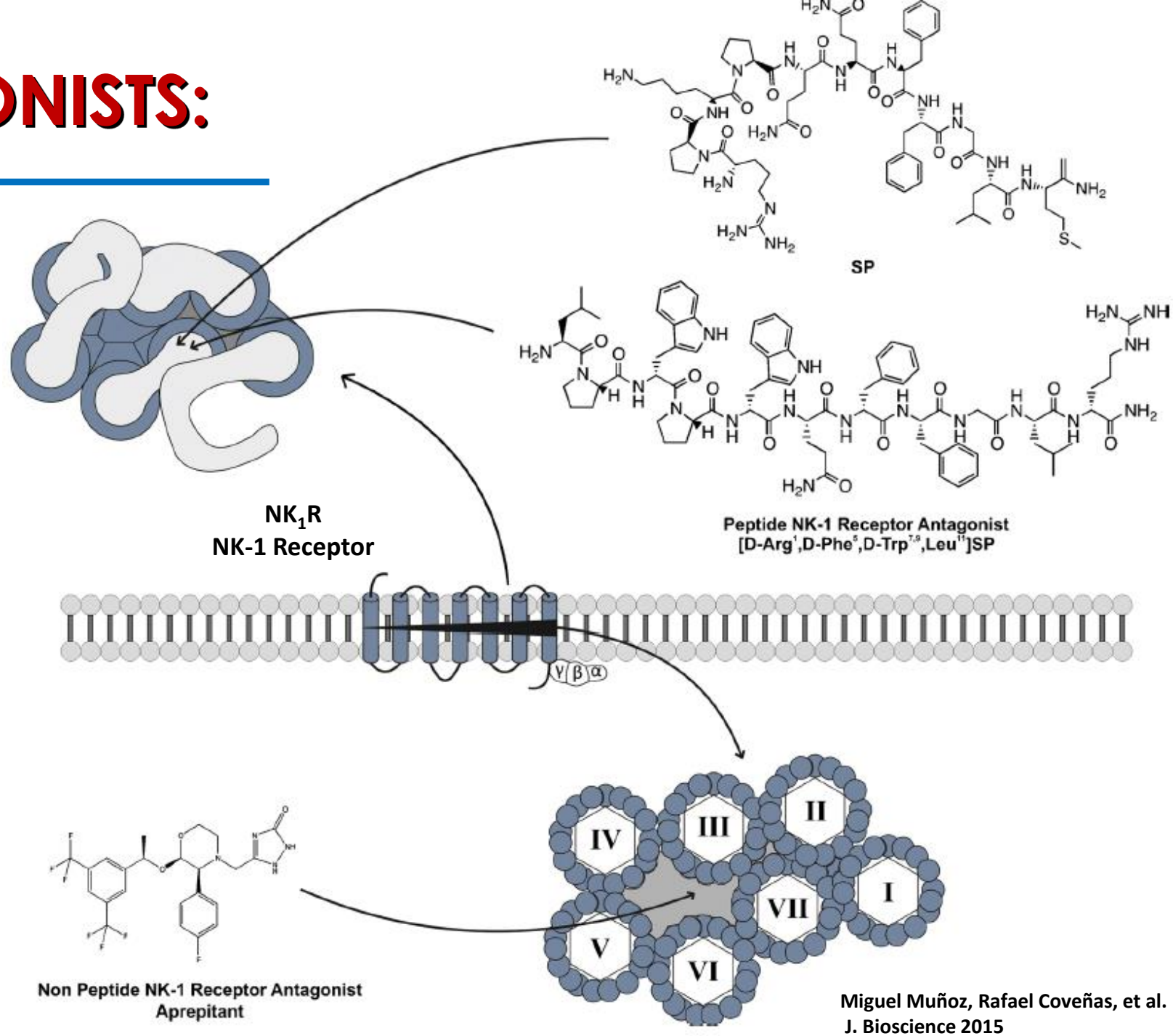
MAIN GOAL:

To obtain in vivo stable diagnostic and therapeutic radiopharmaceuticals for oncological pathologies,

based on well-known NK1R antagonists,

competitive to currently applied Substance P derivatives in nuclear medicine (against glioblastoma multiforme).

NK1R ANTAGONISTS:



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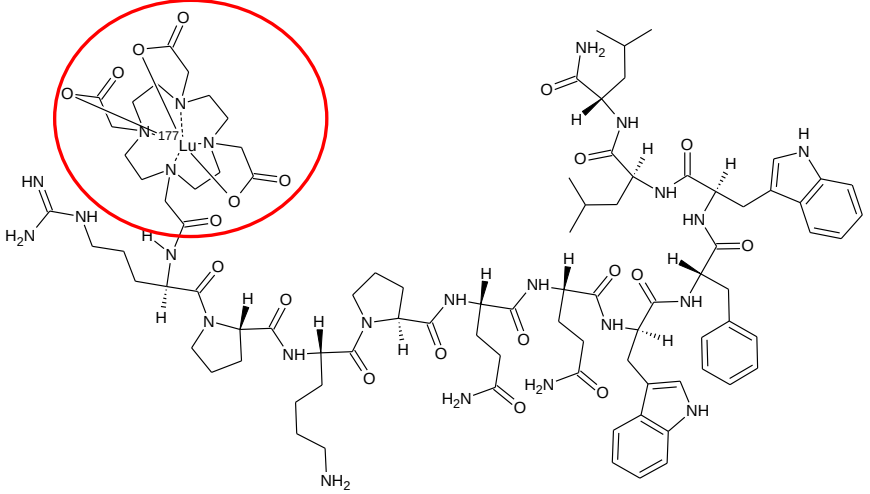
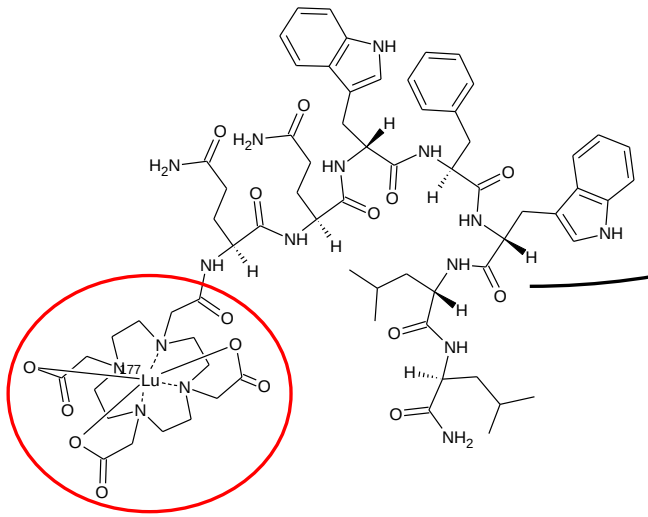


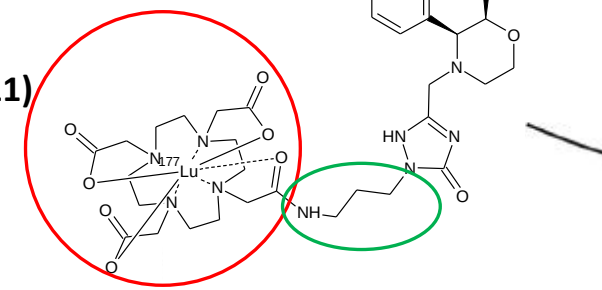
[^{177}Lu]-Lu-DOTA-SPANTIDE I

[^{177}Lu]-Lu-DOTA-[D-Arg^{1},D-Trp^{7,9},Leu^{11}]-Substance P

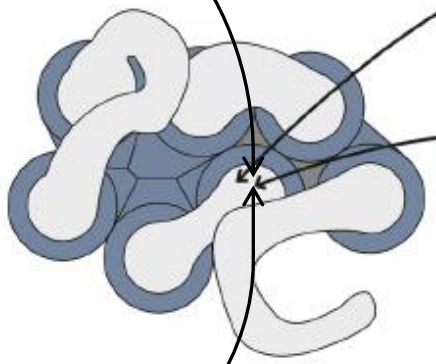


[^{177}Lu]-Lu-DOTA-SPANTIDE I (5-11)

[^{177}Lu]-Lu-DOTA-[D-Trp^{7,9},Leu^{11}]-Substance P (5-11)

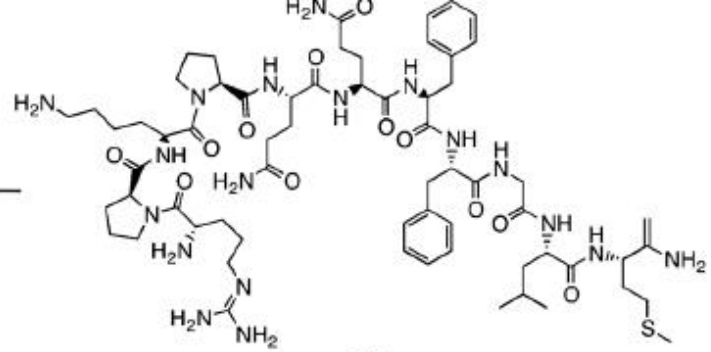


[^{177}Lu]-Lu-DOTA-linker-Aprepitant

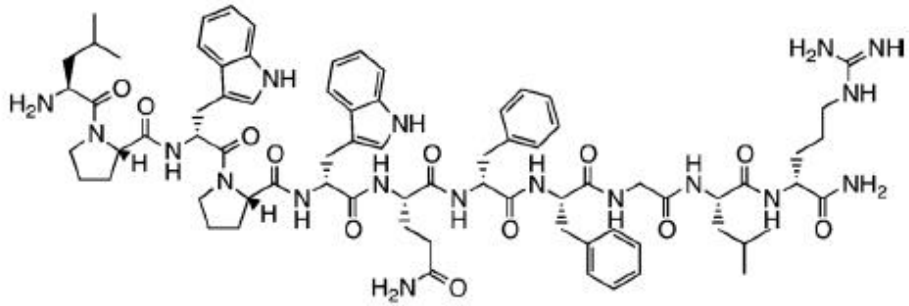


NK$_1$R

NK-1 Receptor

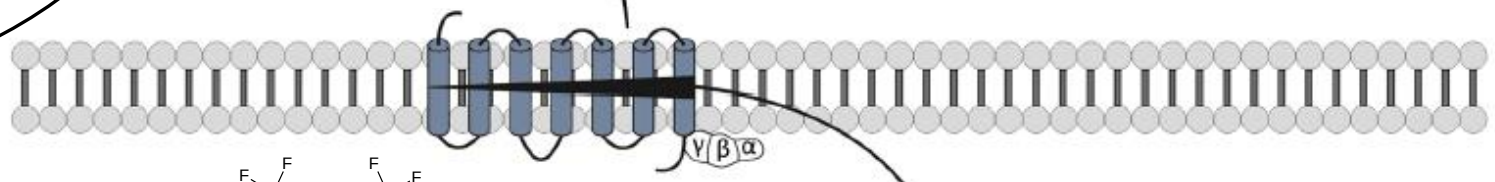


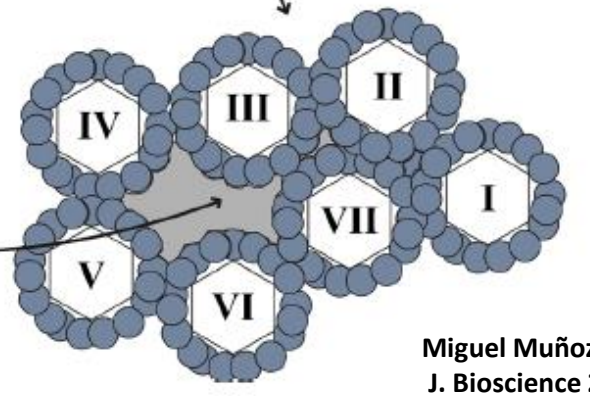
SP



Peptide NK-1 Receptor Antagonist

[D-Arg^{1},D-Phe^{5},D-Trp^{7,9},Leu^{11}]SP





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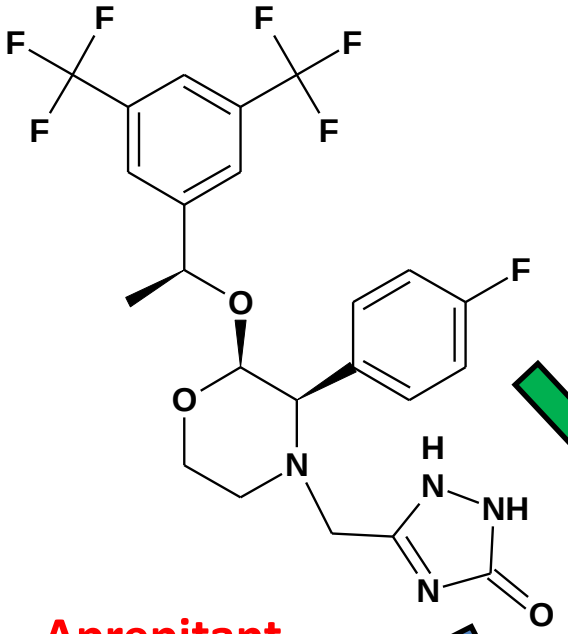
PROJECT IDEA:



Aprepitant
APT

[^{177}Lu]Lu-DOTA-APT

[^{68}Ga]Ga-DOTA-APT

Non-peptide NK1R antagonist

D-Arg-Pro-Lys-Pro-Gln-Gln-D-Trp-Phe-D-Trp-Leu-Leu-NH_2

SPANTIDE I (1-11)

[D-Arg^{1},D-Trp^{7,9},Leu^{11}]-Substance P

[^{177}Lu]Lu-DOTA-SPE (1-11)

[^{68}Ga]Ga-DOTA-SPE (1-11)

versus

Gln-Gln-D-Trp-Phe-D-Trp-Leu-Leu-NH_2

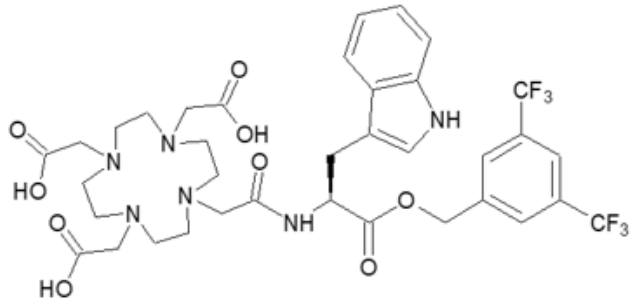
SPANTIDE I (5-11)

[^{177}Lu]Lu-DOTA-SPE (5-11)

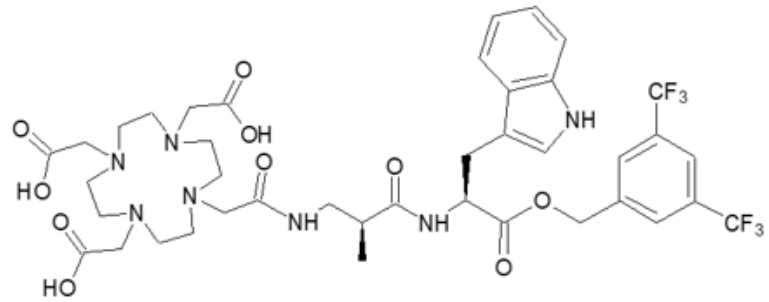
[^{68}Ga]Ga-DOTA-SPE (5-11)

Peptide NK1R antagonists

L732,138:



1d



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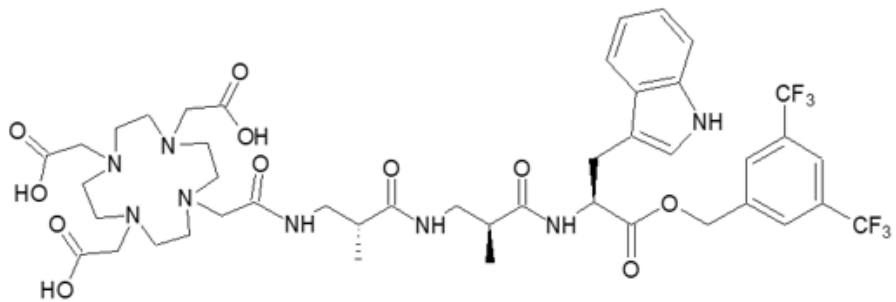
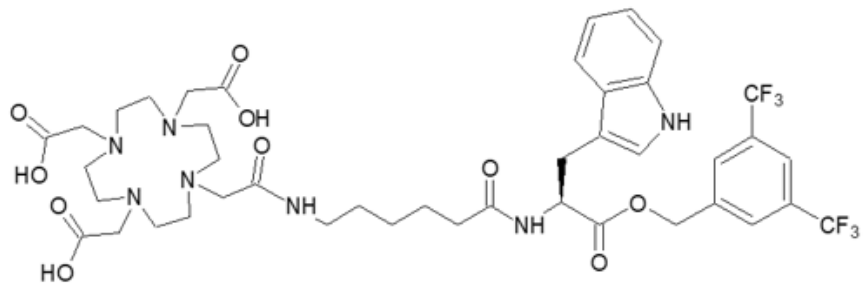


3d



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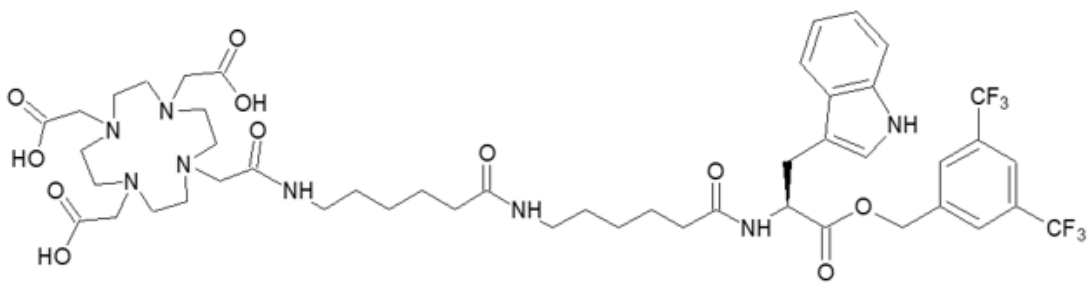
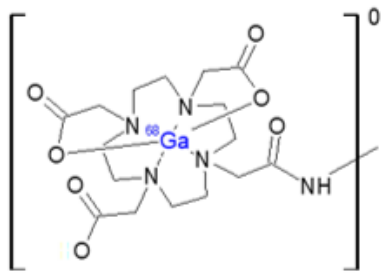
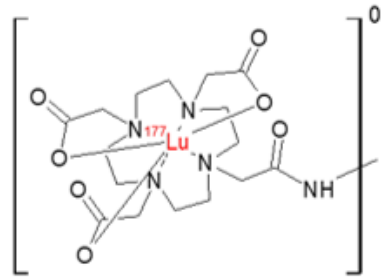


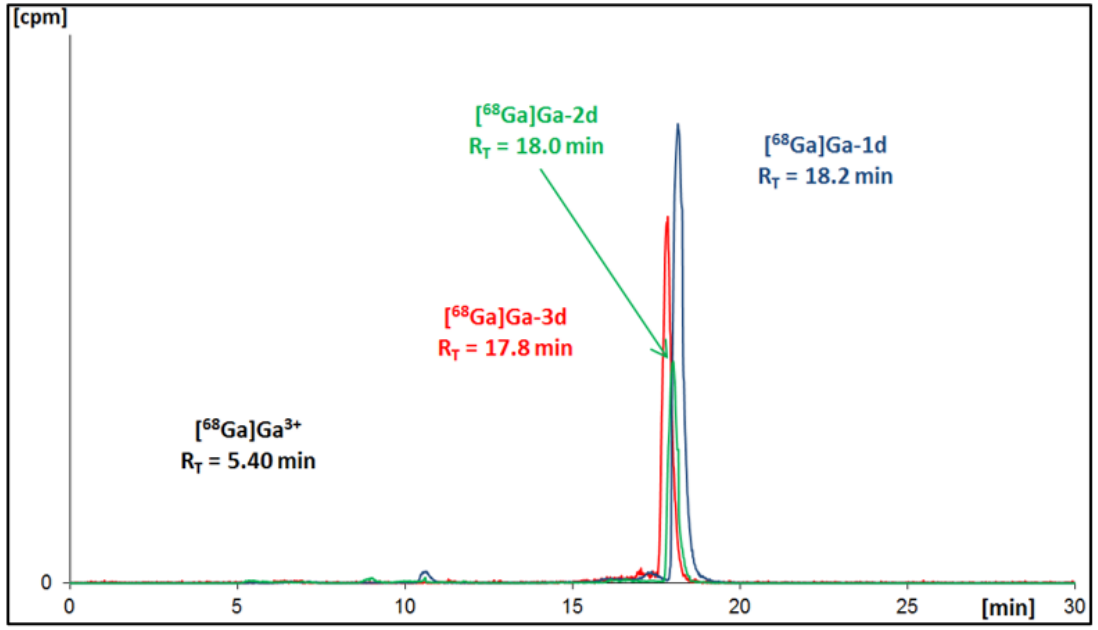
5d



[^{68}Ga]Ga-DOTA-



[^{177}Lu]Lu-DOTA-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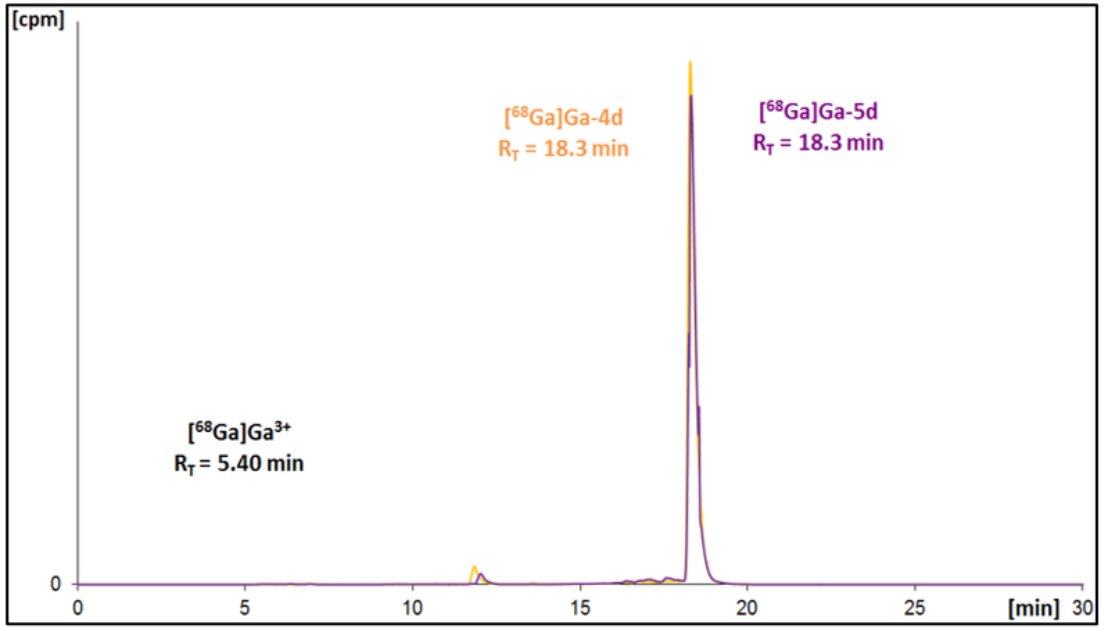
[68Ga]Ga-1d
RT = 18.2 min
[68Ga]Ga-3d
RT = 17.8 min
[68Ga]Ga3+
RT = 5.40 min
0
0 5 10 15 20 25 [min] 30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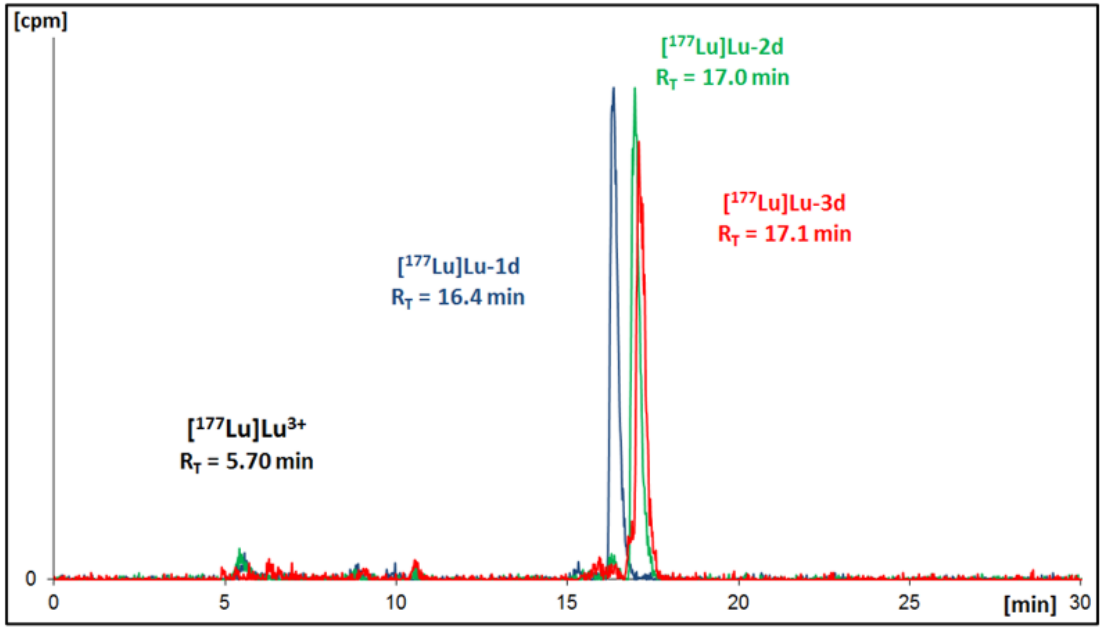
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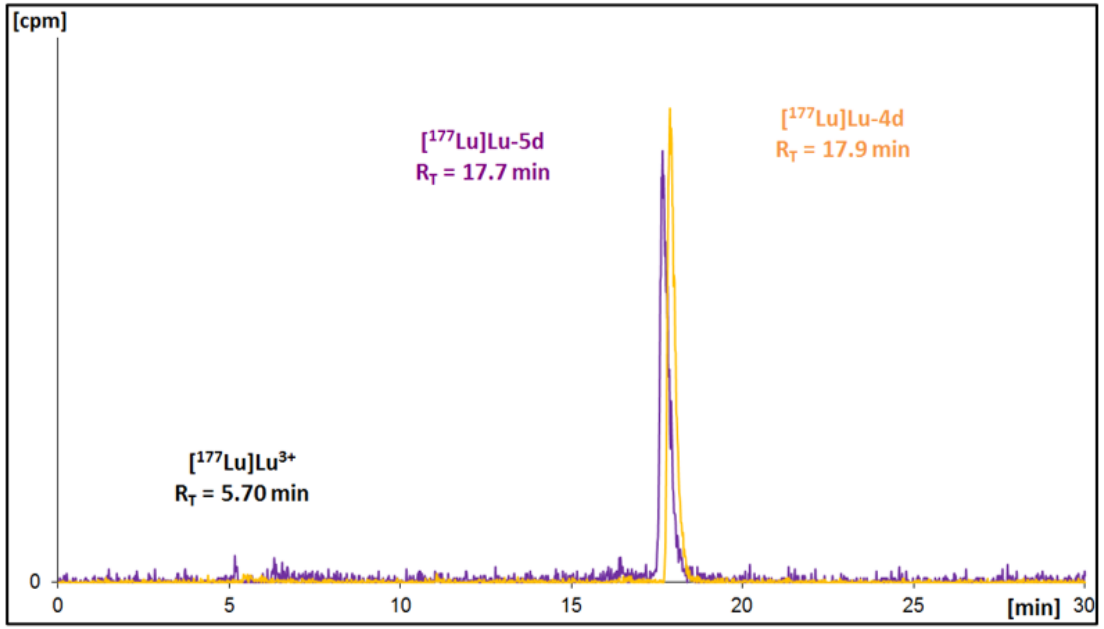
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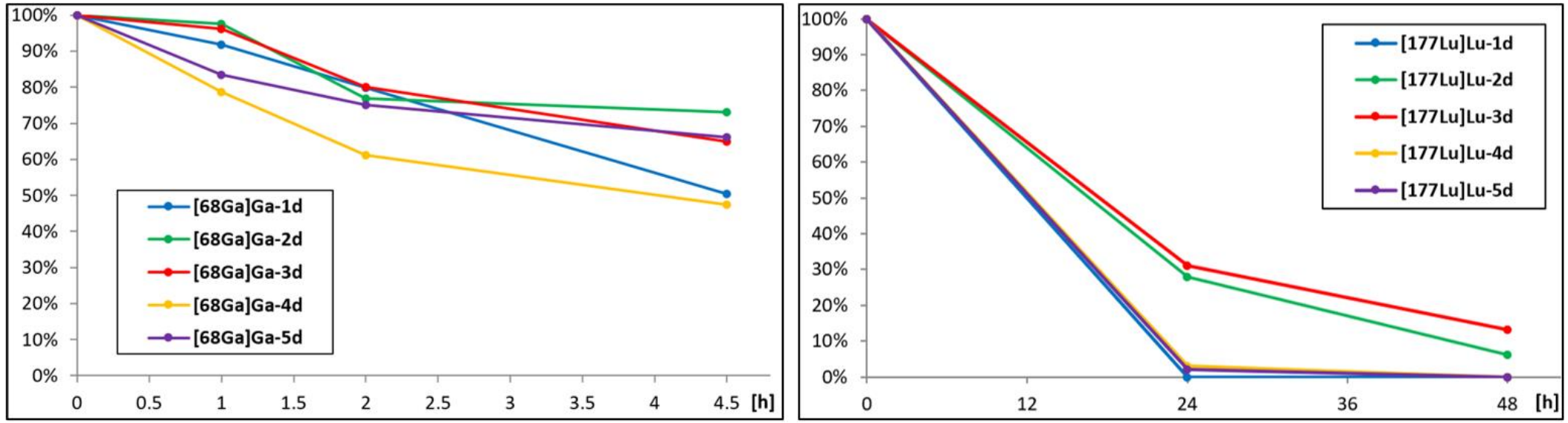


Figure 4. Percentage of intact ^{68}Ga-radioconjugates (**left**) and ^{177}Lu-radioconjugates (**right**) determined at specific time points during incubation in human serum.

Table 3. LogD values of all radioconjugates determined in *n*-octanol/PBS buffer system.

Radioconjugate	logD (SD)[1]	
	^{68}Ga-	^{177}Lu-
1d-	-0.085 (0.015)	0.400 (0.004)
2d-	-0.060 (0.020)	0.704 (0.005)
3d-	-0.259 (0.017)	0.619 (0.007)
4d-	0.071 (0.023)	0.866 (0.019)
5d-	-0.466 (0.016)	0.294 (0.013)

[1]logD values are presented as means of three independent experiments done in duplicate with the standard deviation in brackets.

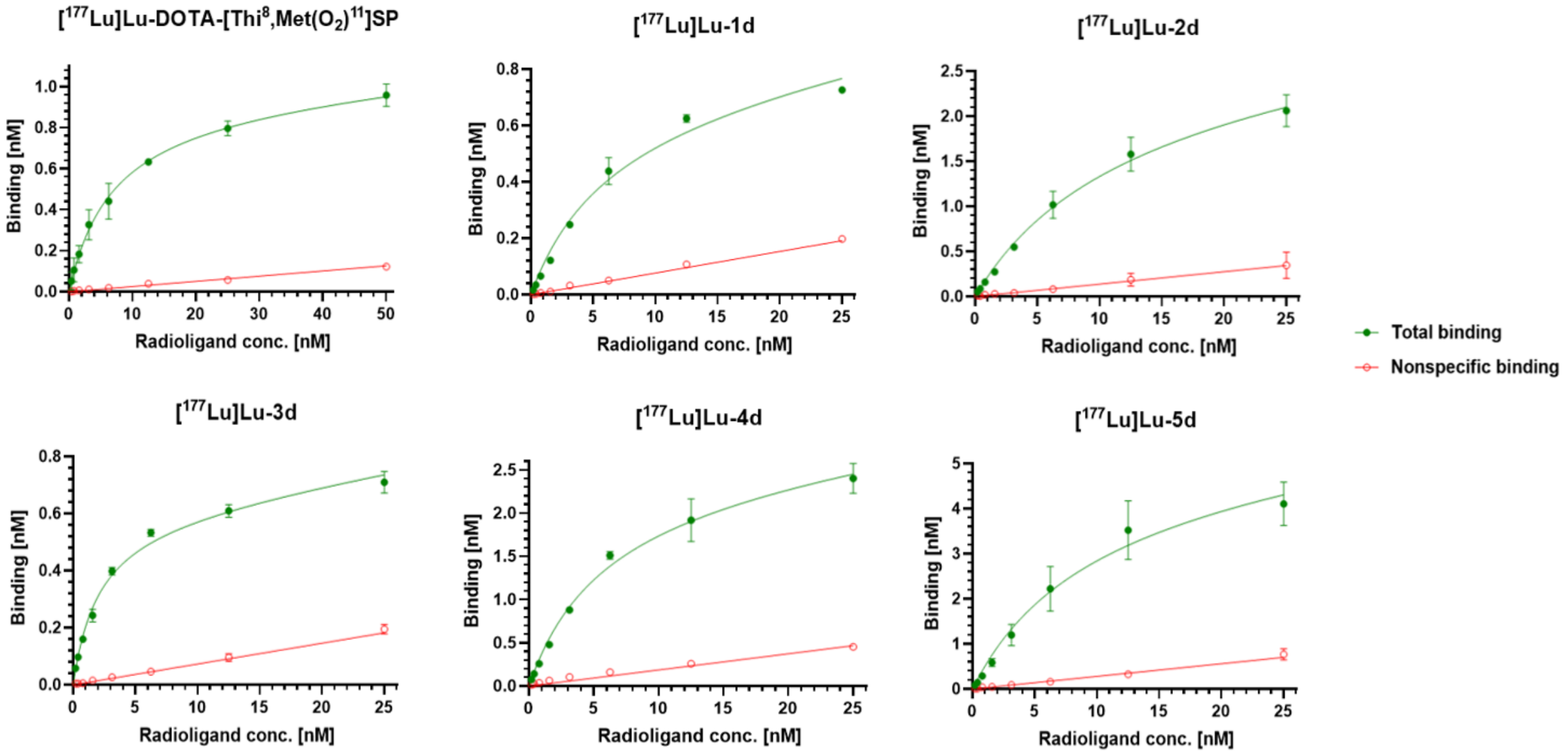
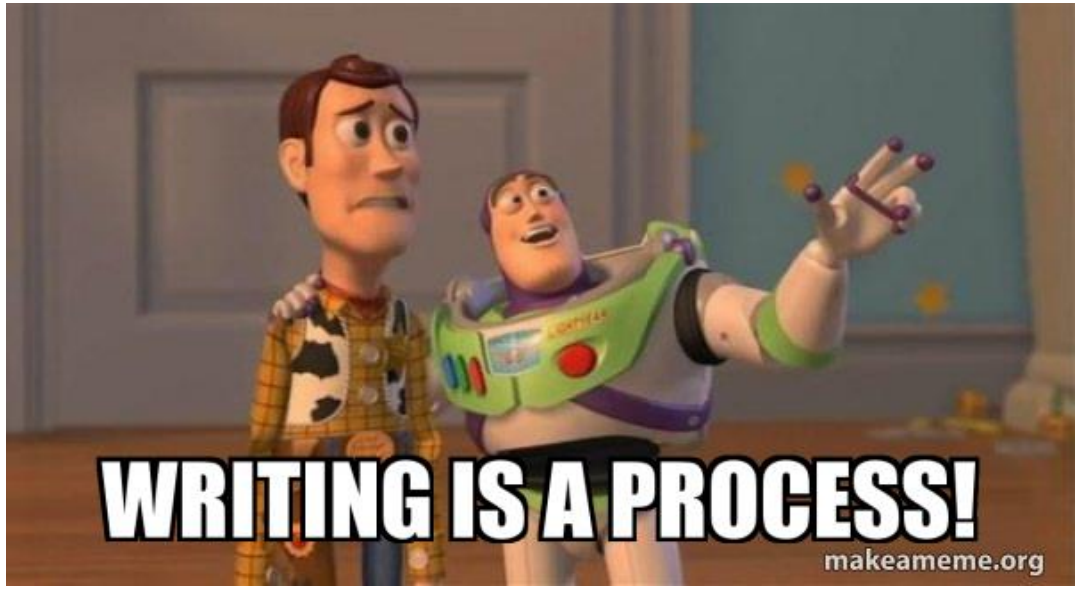


Figure 5. Illustrative binding profiles of ^{177}Lu-radioconjugates of Substance P or L-732,138 derivatives.

THIS YEAR PLANS:

1. Publish recent results

2. Write a dissertation



THANK YOU