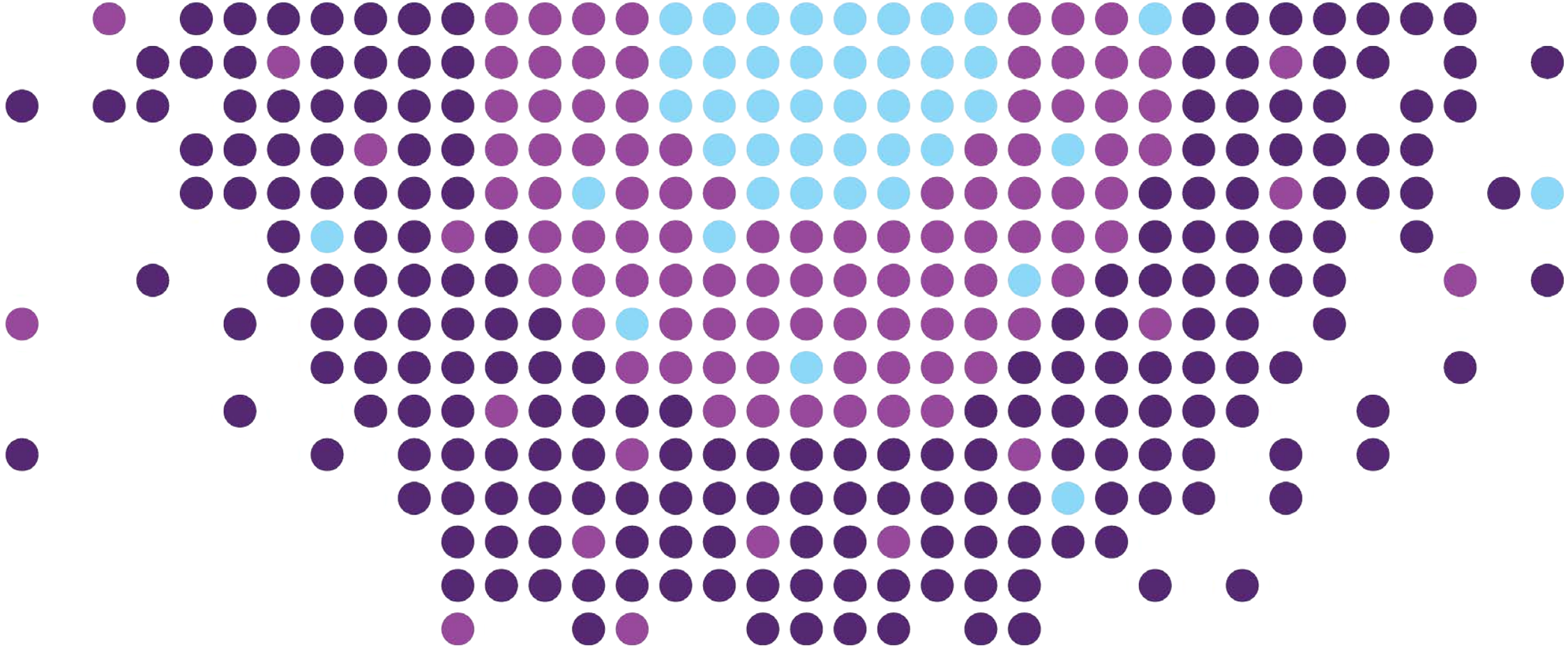
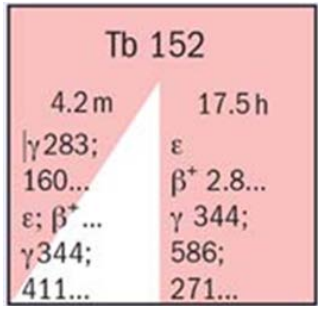


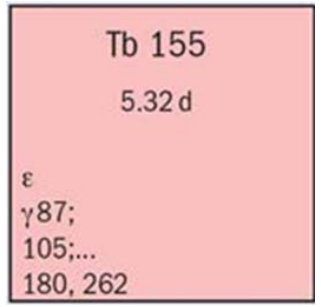
Maarten Ooms – 20/01/2022

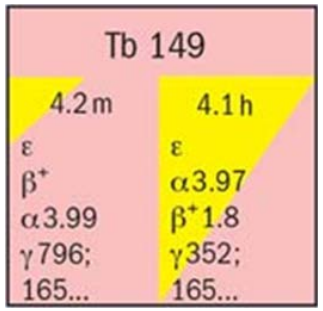
sck cen
Belgian Nuclear Research Centre

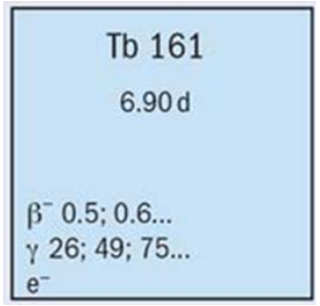
Terbium-161, a high potential emerging isotope in targeted radionuclide therapy

Terbium: the ultimate theranostic element



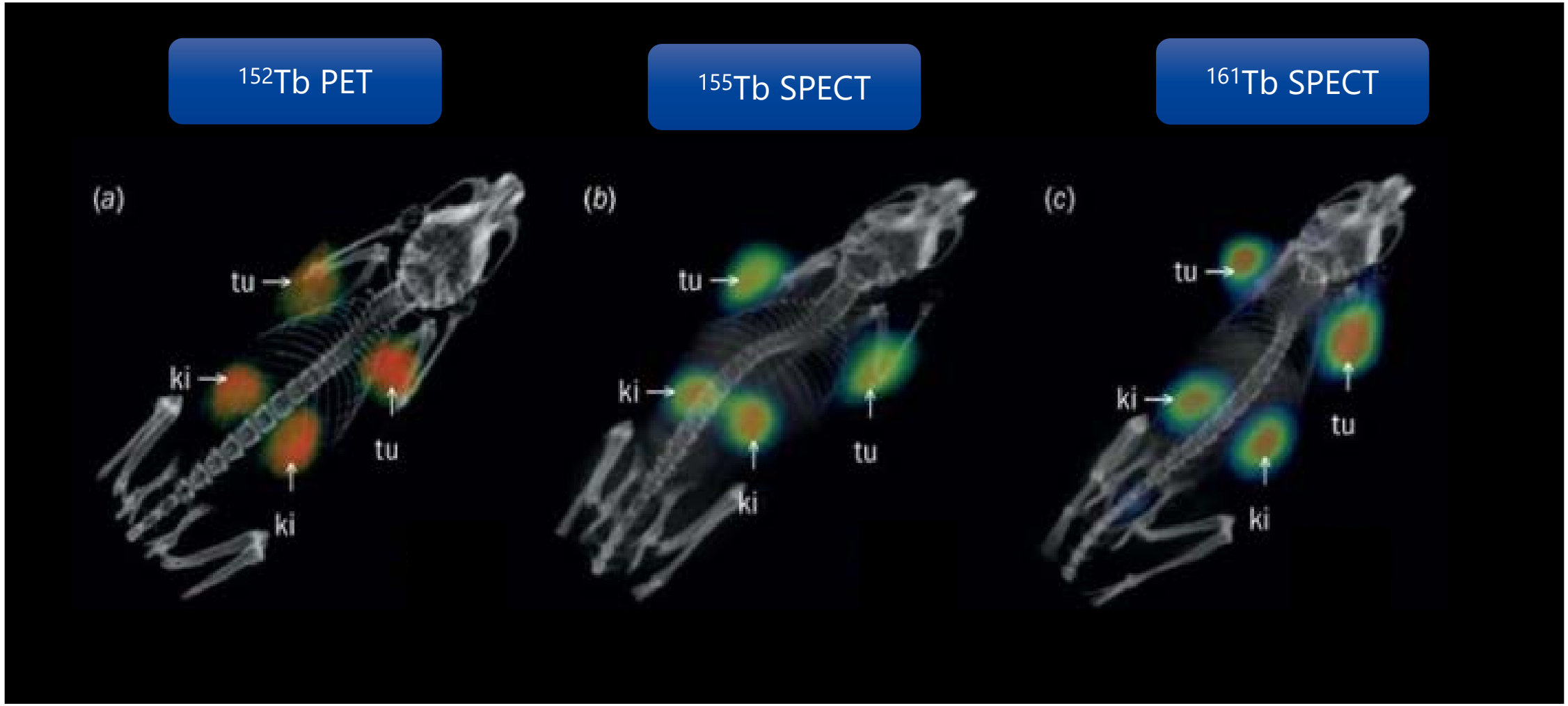






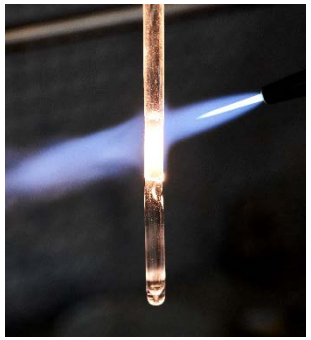
	β^+ $T_{1/2}$ = 17.5h	γ $T_{1/2}$ = 5.3d	α/β^+ $T_{1/2}$ = 4.1h	$\beta^- + \gamma$ $T_{1/2}$ = 6.9d
Fluorescent luminescence	PET imaging	SPECT imaging	α Therapy	β Therapy

Imaging potential of Terbium isotopes



Müller et al. JNM, 53 (12), 1951 – 1959 (2012)

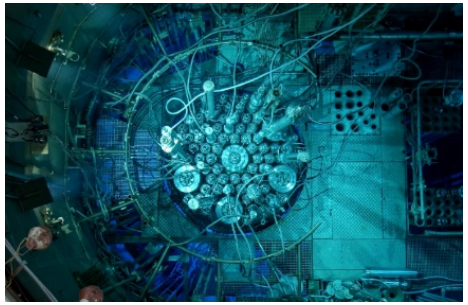
Production of Tb-161



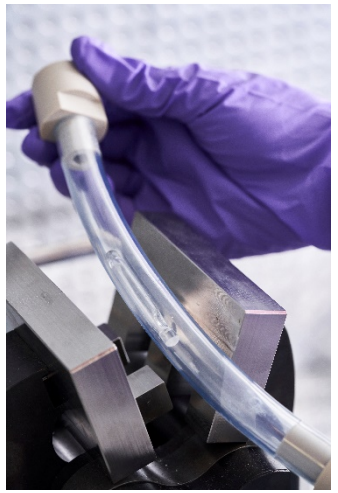
^{160}Gd target material

^{160}Gd (n,γ) ^{161}Gd ➔ ^{161}Tb

Neutron irradiation



^{160}Gd + ^{161}Tb



Radiochemical Tb/Gd separation

Purified Tb-161

^{160}Gd Recycling

Therapeutic potential of Tb-161

- **Chemically comparable to Lu-177**
- **Similar physical properties (half life, beta energy,…)**
- **High emission of Auger electrons ➔ higher potential?**

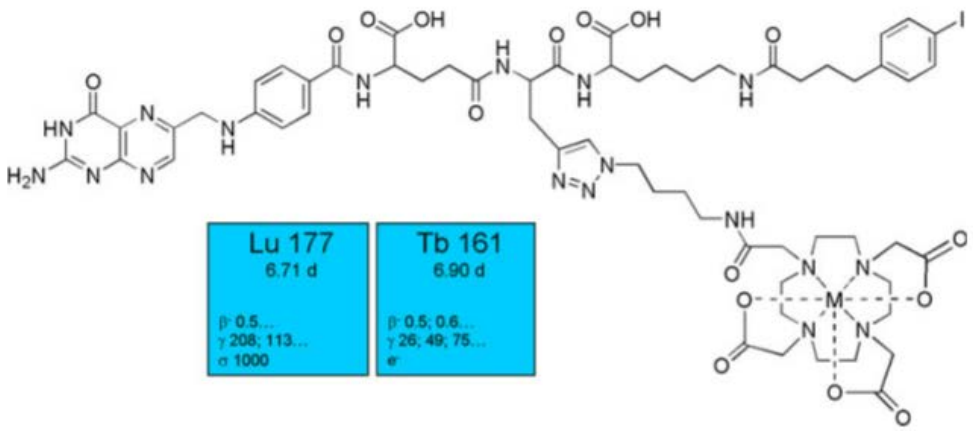
Table 1 Comparison of the decay properties of ^{177}Lu and ^{161}Tb

Isotope	^{177}Lu	^{161}Tb
Nuclide availability	Good	Limited
ß$^-$-energy av/decay (intensity)	134 keV (100 %)	154 keV (100 %)
Conversion and Auger electrons (intensity)	3–50 keV (14 %)	3–50 keV (224 %)
Eγ/E$_X$ (intensity)	208 keV (10 %)	75 keV (10 %)
	113 keV (6 %)	45–53 keV (39 %)
Half life	6.7 days	6.9 days

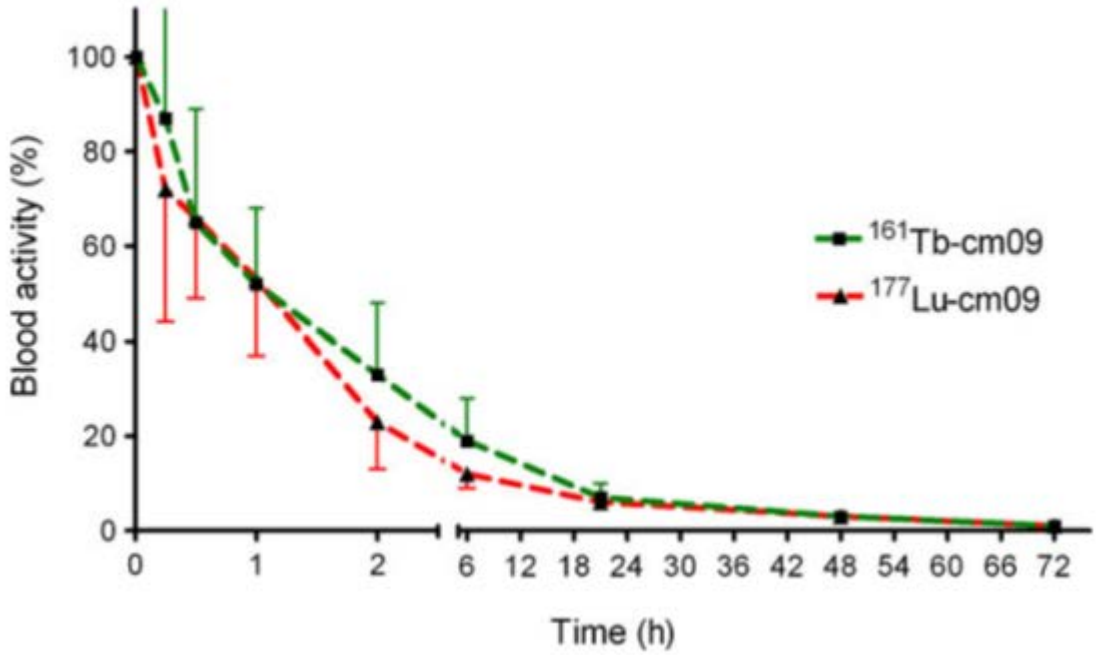
Data from: National Nuclear Data Centre Brookhaven National Laboratories

Haller et al. EJNMMI Research (2016) 6:13

Tb-161: a high potential alternative for Lu-177



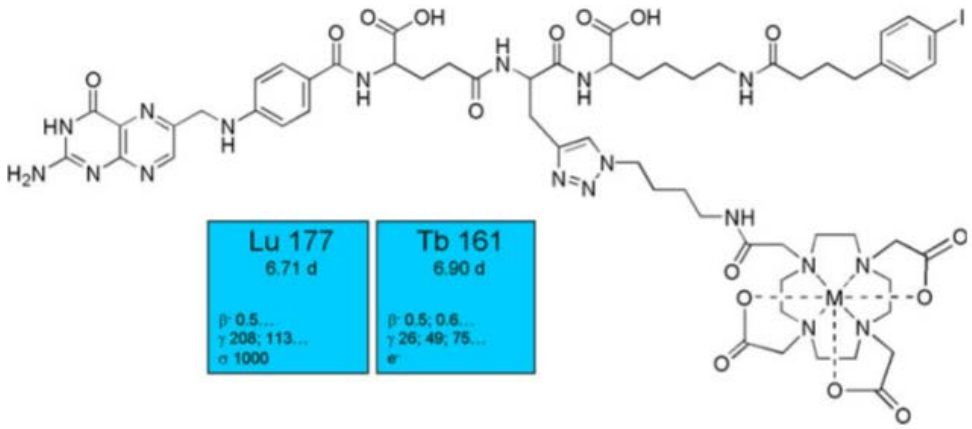
^{177}Lu & ^{161}Tb radiolabeled folate derivative



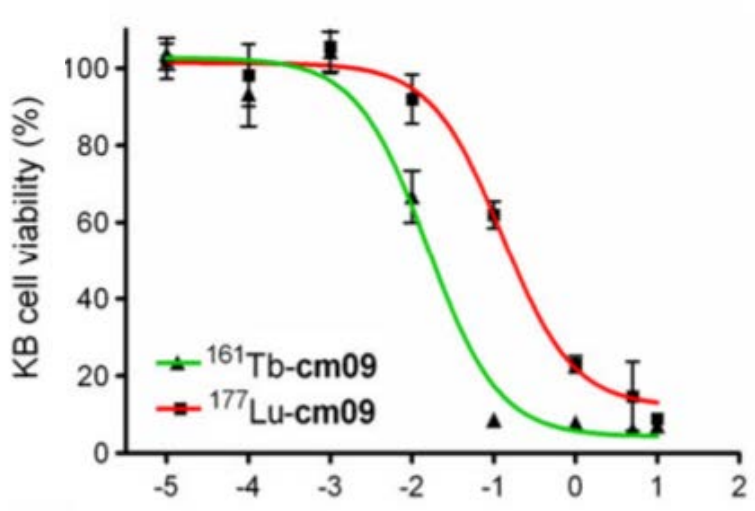
Comparable pharmacokinetics

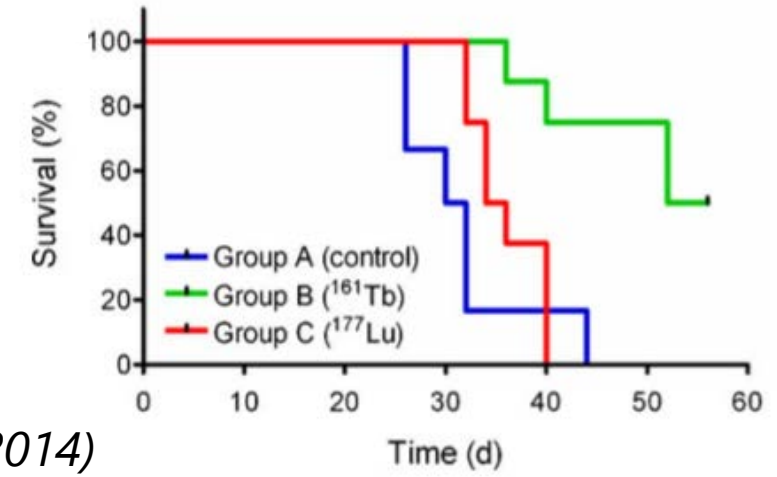
Müller et al. EJNMMI, 41: 476 – 485 (2014)

Tb-161: a high potential alternative for Lu-177



^{177}Lu & ^{161}Tb radiolabeled folate derivative





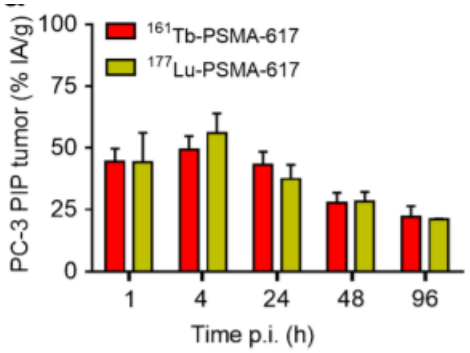
Müller et al. EJNMMI, 41: 476 – 485 (2014)

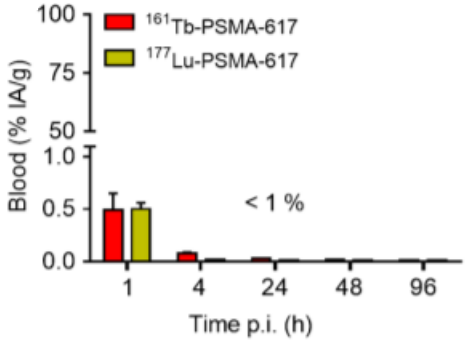
European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:1919–1930
https://doi.org/10.1007/s00259-019-04345-0

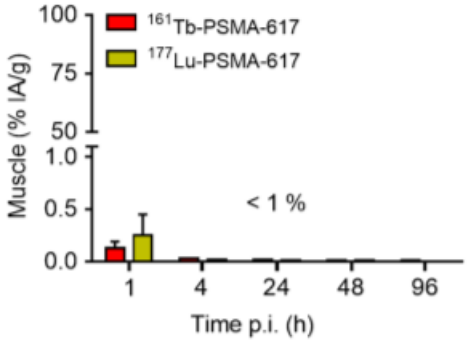
ORIGINAL ARTICLE

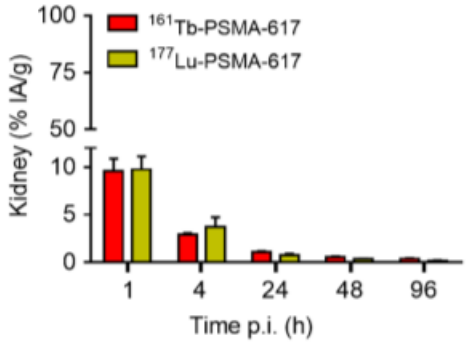
Terbium-161 for PSMA-targeted radionuclide therapy of prostate cancer

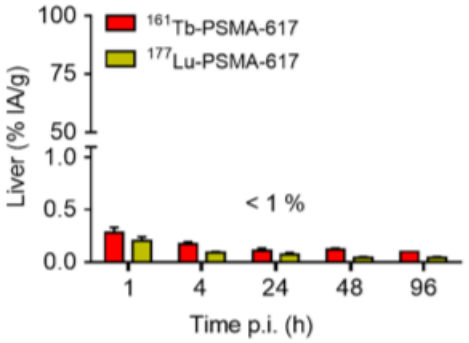
Cristina Müller[1] · Christoph A. Umbricht[1] · Nadezda Gracheva[1] · Viviane J. Tschan[1] · Giovanni Pellegrini[2] · Peter Bernhardt[3] · Jan Rijn Zeevaart[4] · Ulli Köster[5] · Roger Schibli[1,6] · Nicholas P. van der Meulen[1,7]

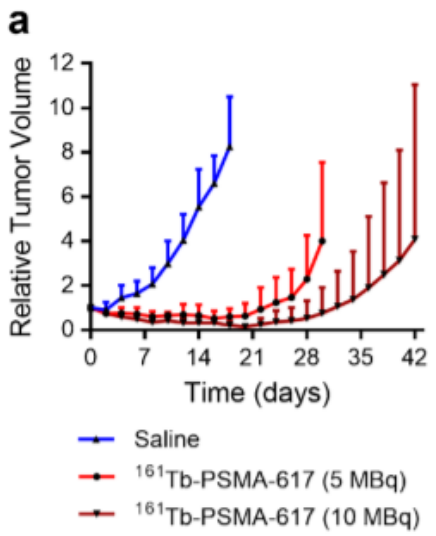


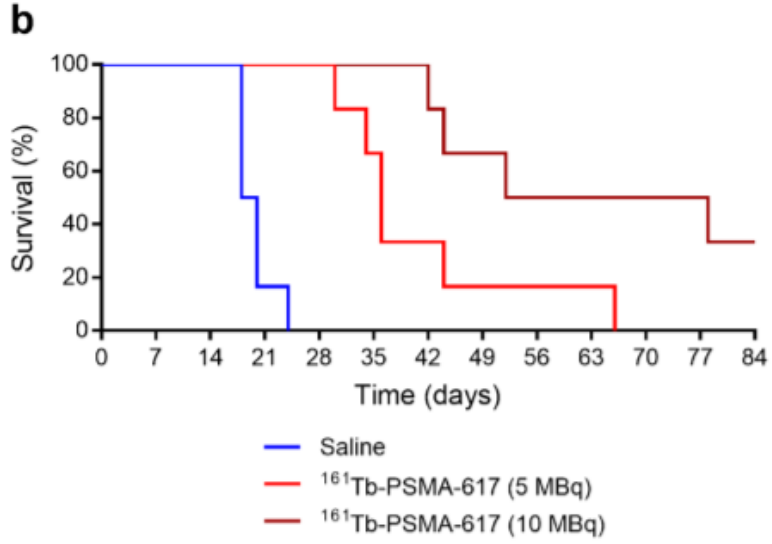












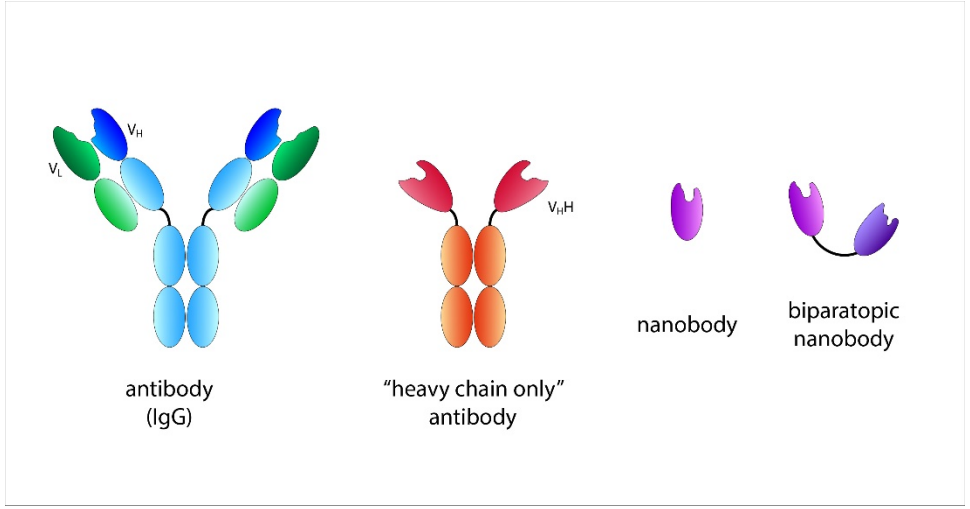
Extending the potential of Tb-161

- Current research limited to well known carriers using established reaction conditions

  (DOTATATE, PSMA 617, folate, …)

90°C
15 min

- Increasing interest in more innovative carriers



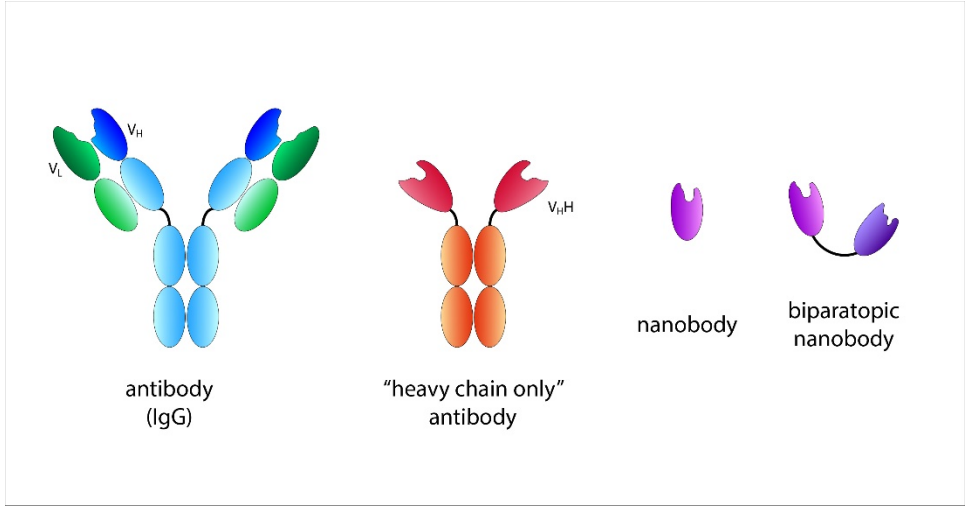
Extending the potential of Tb-161

- Current research limited to well known carriers using established reaction conditions

  (DOTATATE, PSMA 617, folate, …)

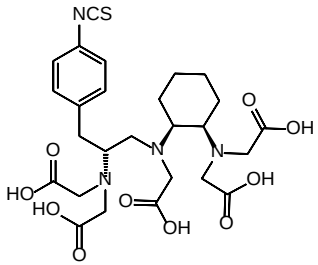
- Increasing interest in more innovative carriers

Harsh radiolabeling conditions incompatible with heat sensitive molecules

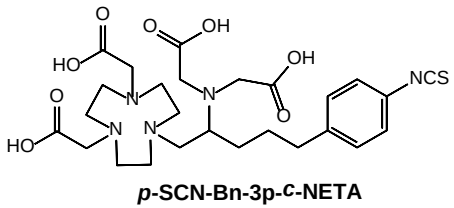


The quest for innovative radiolabeling methods

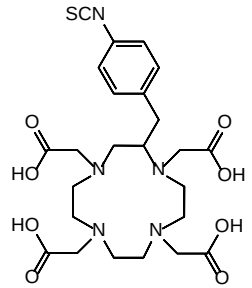
Irwin Cassells



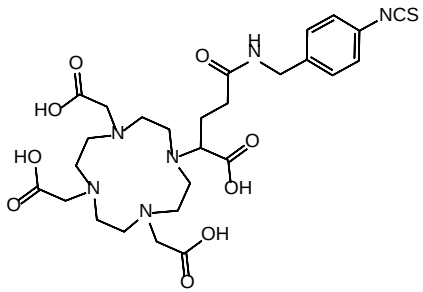
p-SCN-Bn-CHX-A"-DTPA



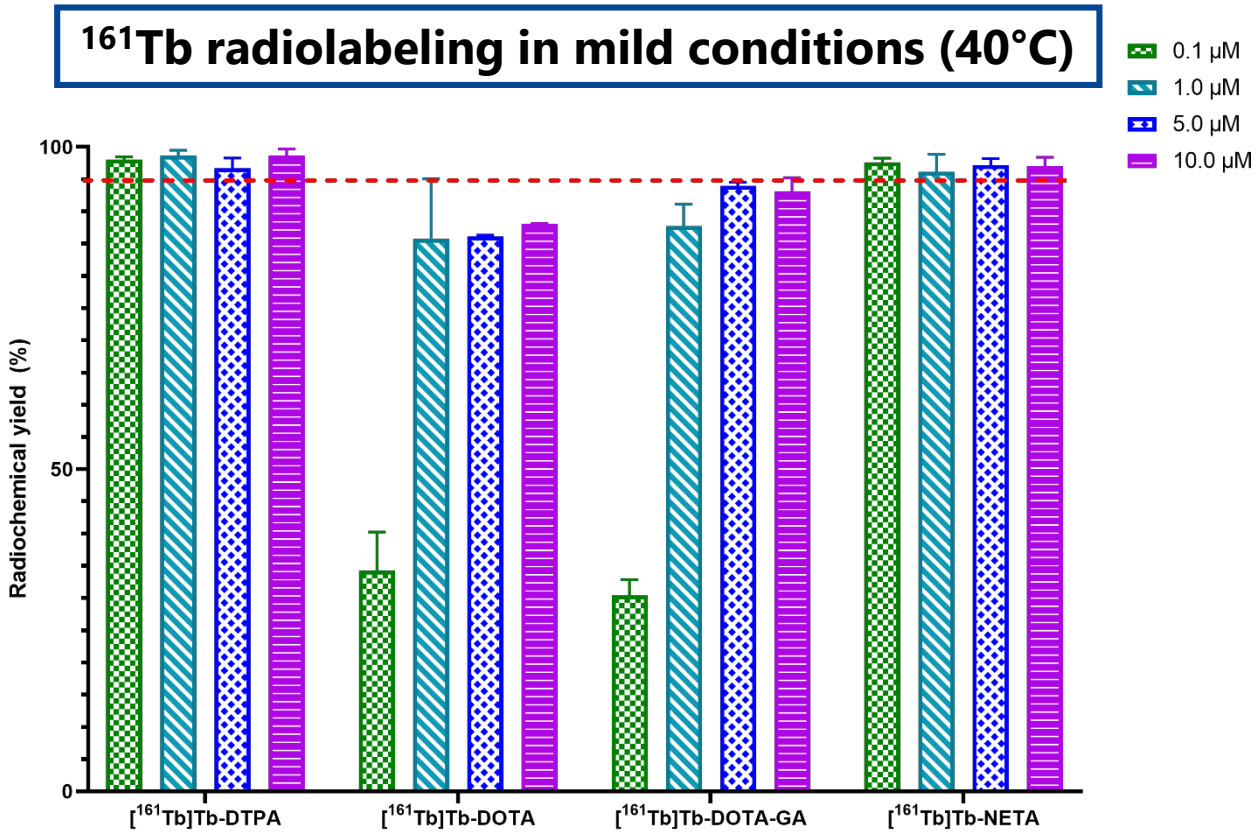
p-SCN-Bn-3p-*c*-NETA



p-SCN-Bn-DOTA



p-SCN-Bz-DOTA-GA

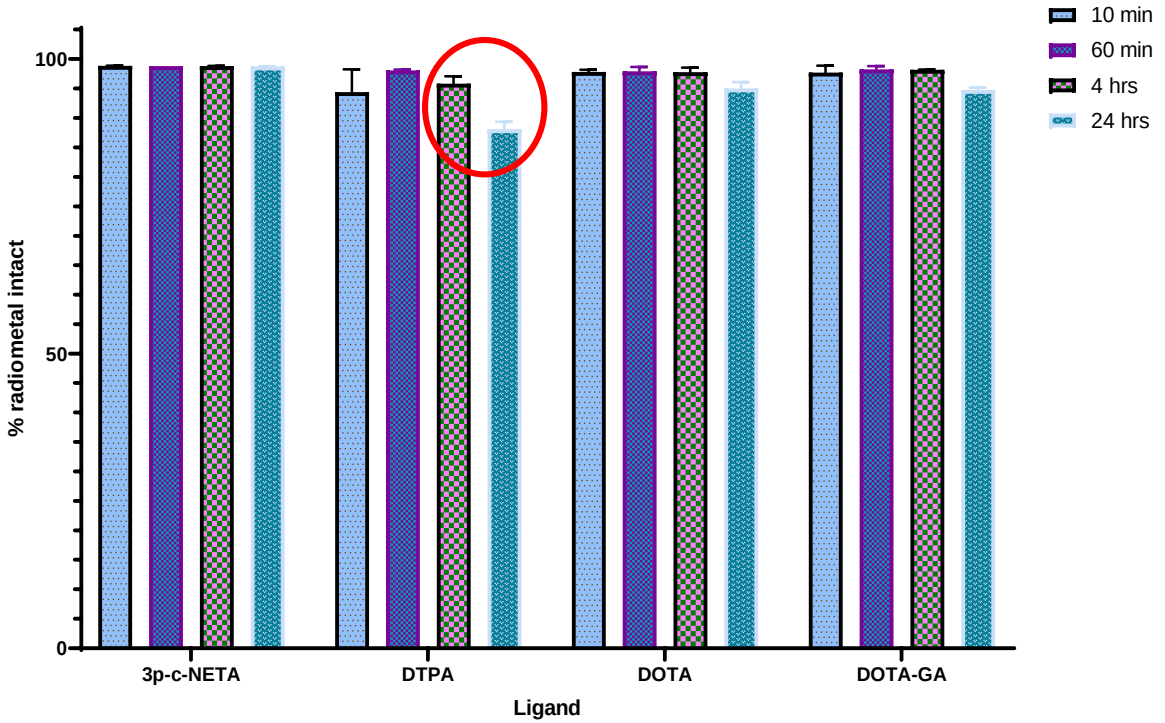


Cassells et al. Front Med, 8, (2021)

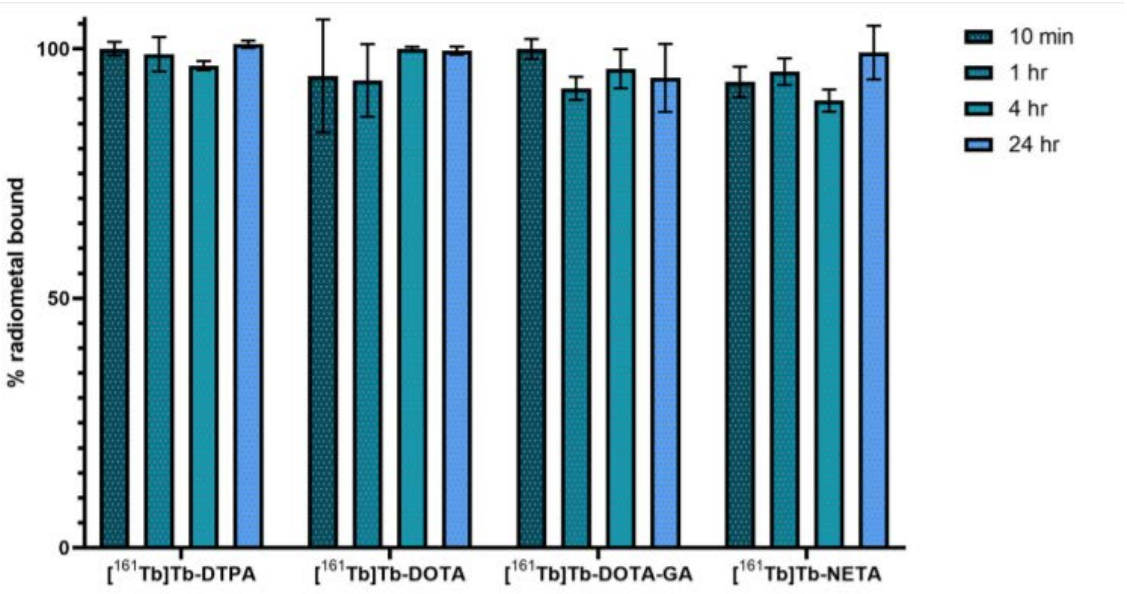
The quest for innovative radiolabeling methods

Irwin Cassells

In vitro stability (human serum)

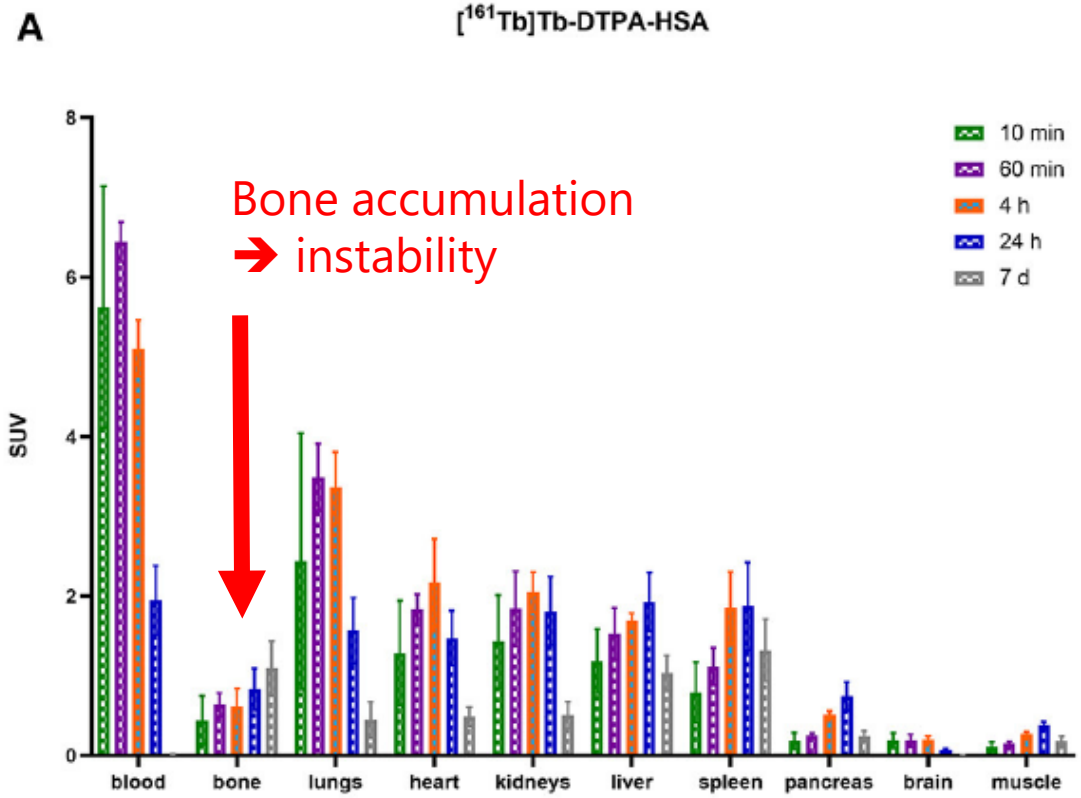


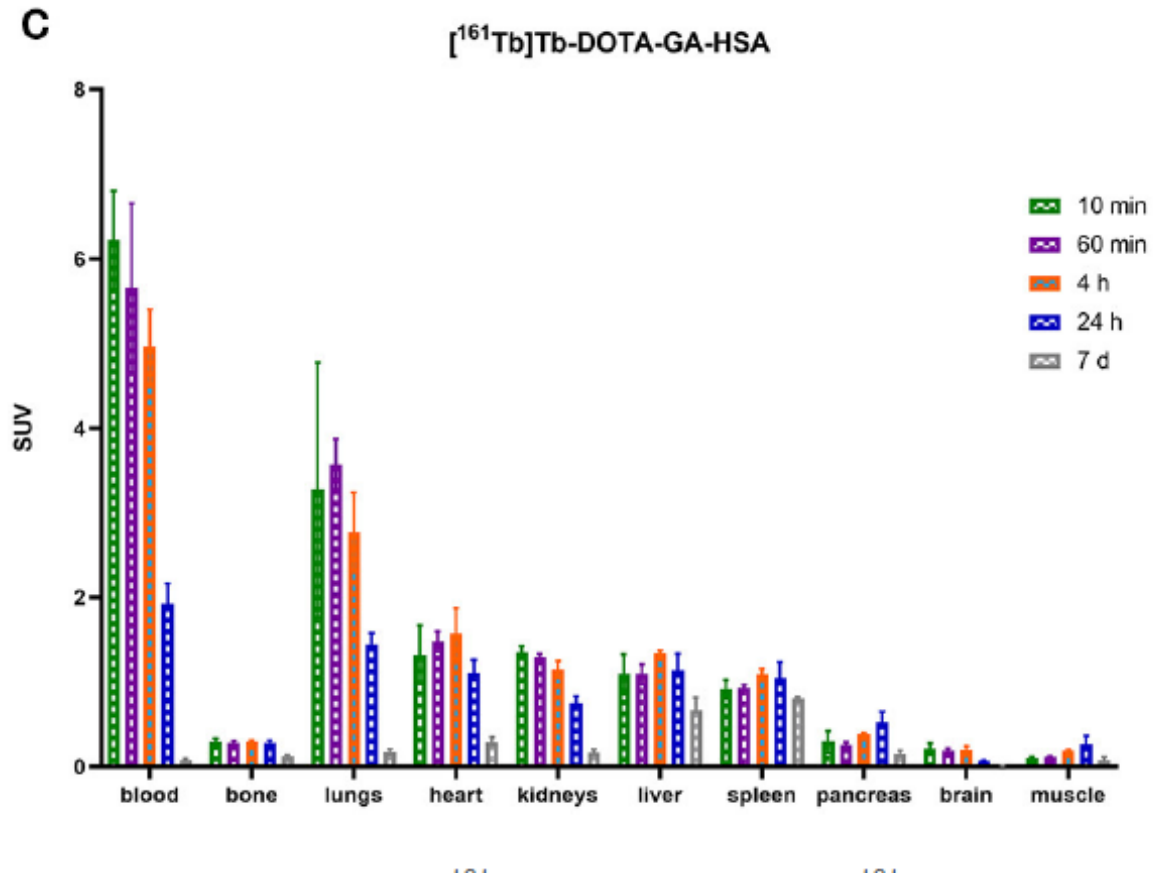
In vitro stability (PBS)



Cassells et al. Front Med, 8, (2021)

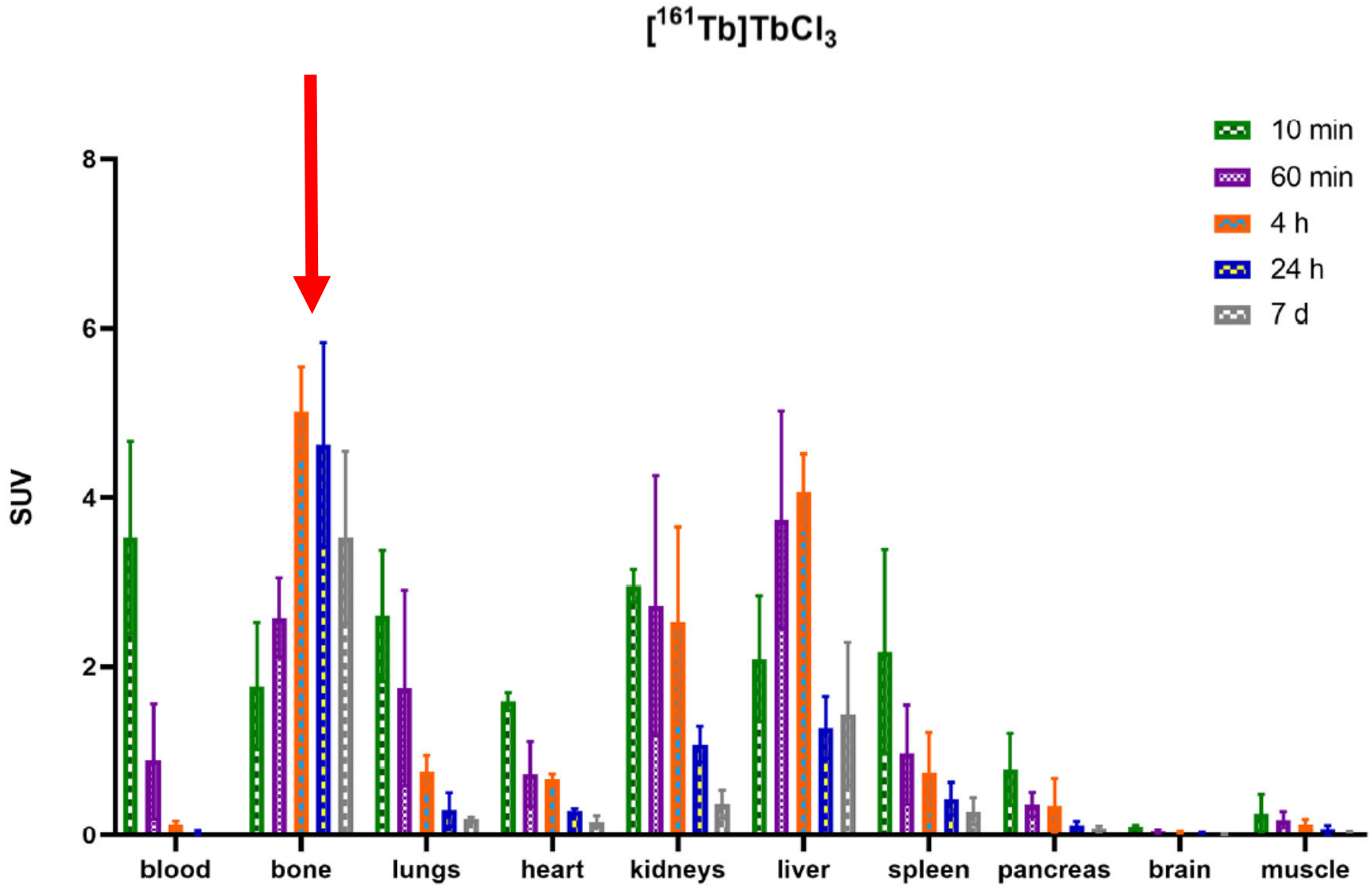
The quest for innovative radiolabeling methods





Cassells et al. Front Med, 8, (2021)

The quest for innovative radiolabeling methods



Cassells et al. Front Med, 8, (2021)

Maximizing the Auger Potential

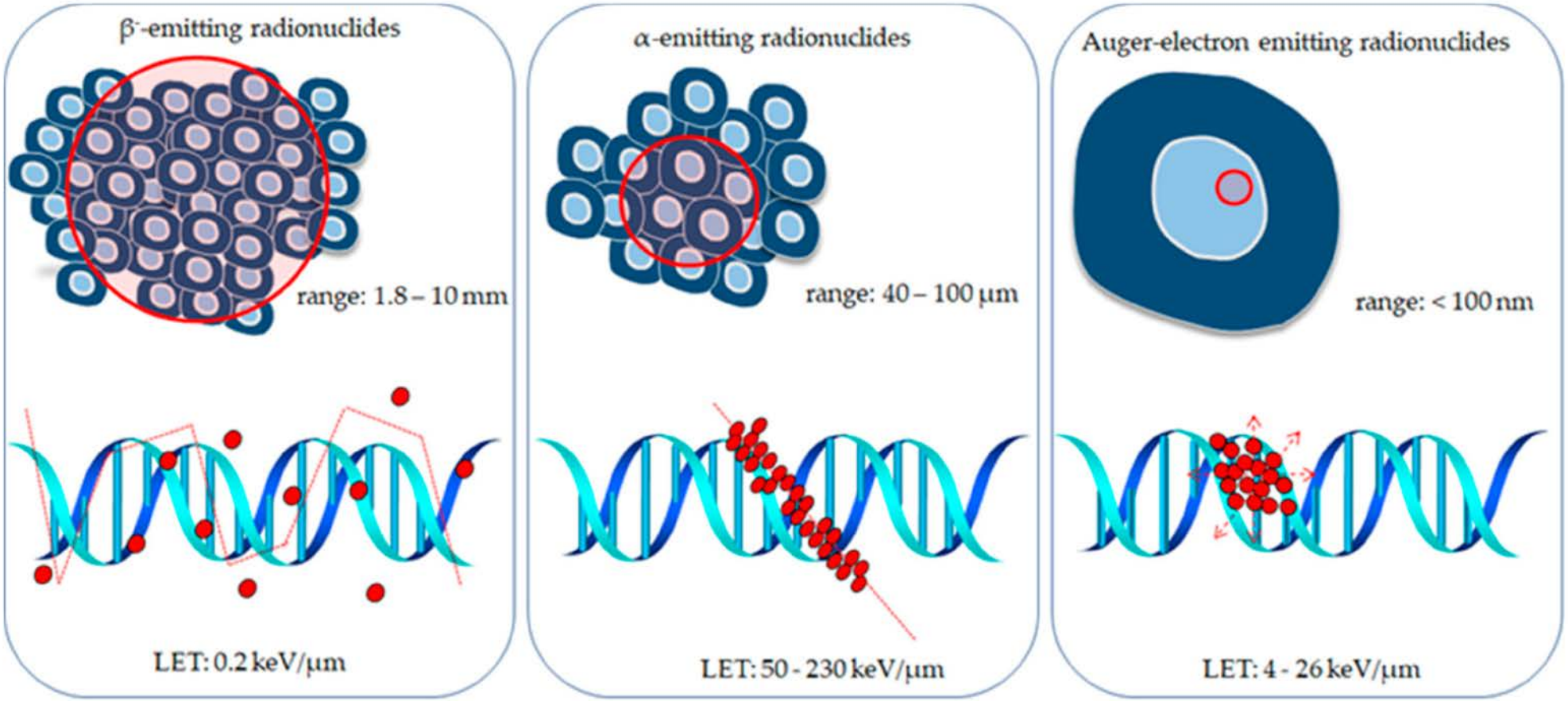


Figure from: Czerwińska et al. Molecules, 25(7), 1743(2020)

Internalization and intracellular targeting is crucial

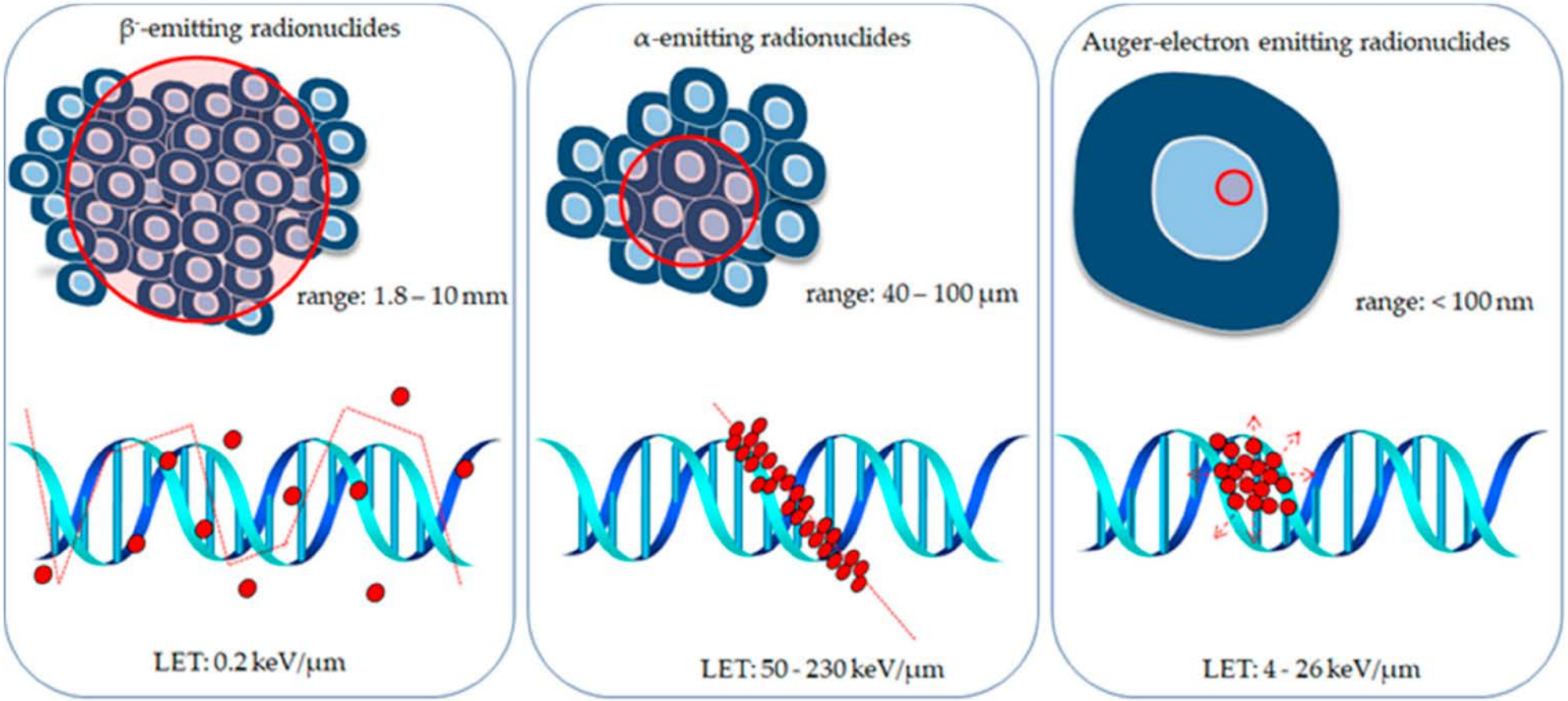
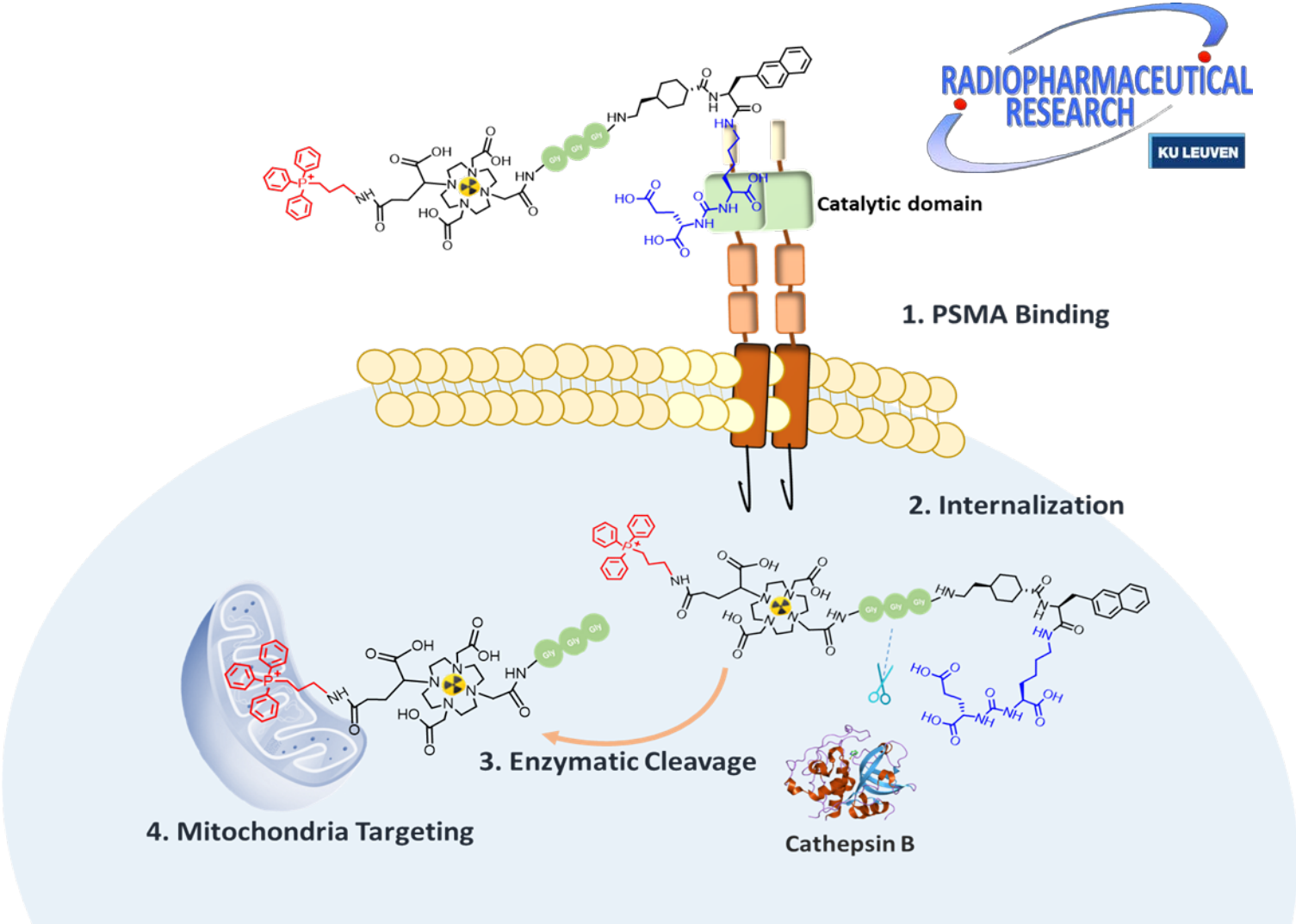


Figure from: Czerwińska et al. Molecules, 25(7), 1743(2020)

Maximizing the Auger Potential

- Specific delivery of therapeutic radionuclides to radiosensitive organelles (nucleus or mitochondria)
- Enhancement of radiotherapeutic effects at lower doses.
- Maximizing the potential of Auger electrons

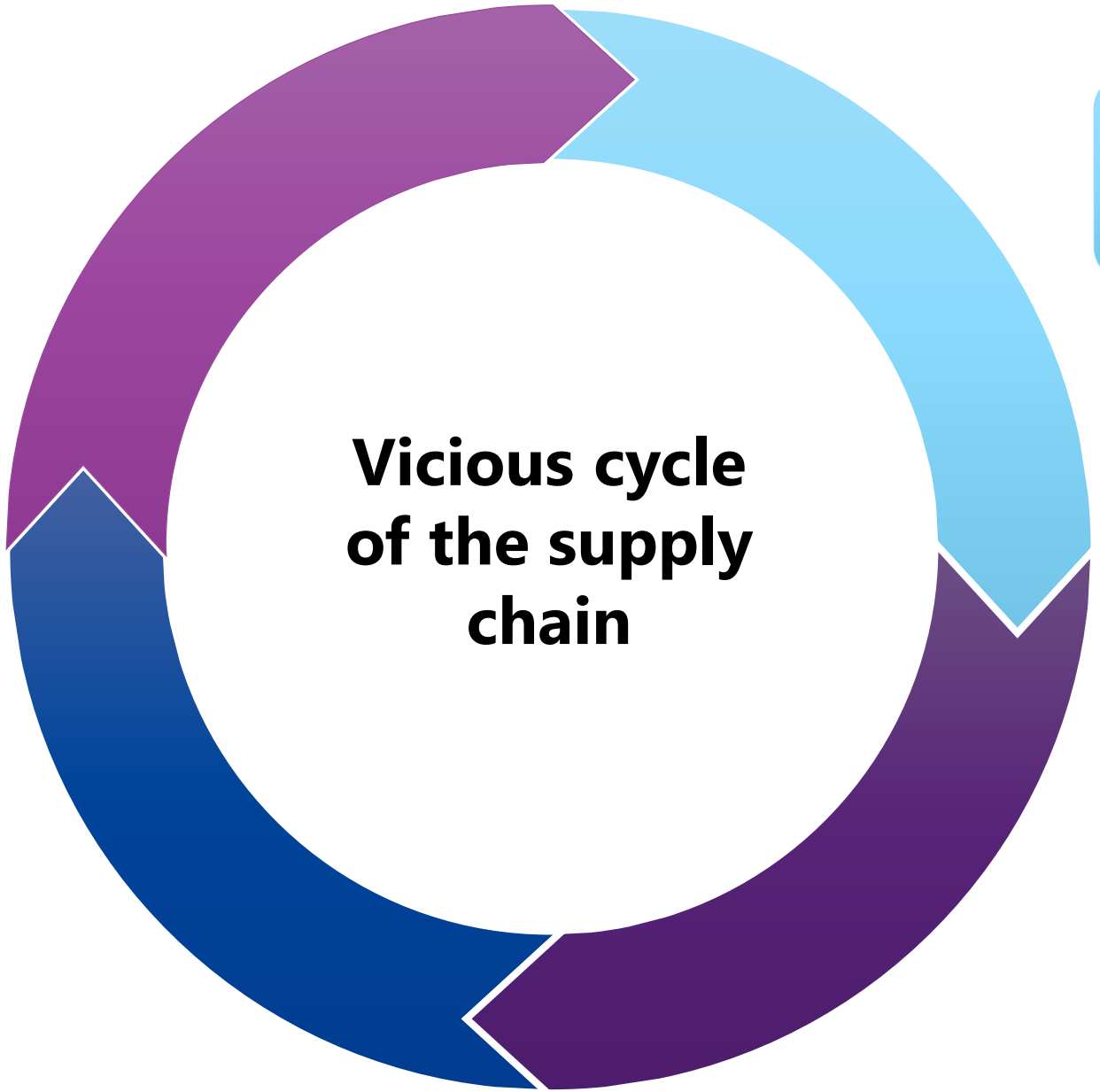


Conclusions

- Tb-161 is a high potential therapeutic alternative for Lu-177
- High abundance of Auger emitters = high therapeutic effect
- Internalization = crucial to capitalize on this effect
- Supply of Tb-161 is still problematic

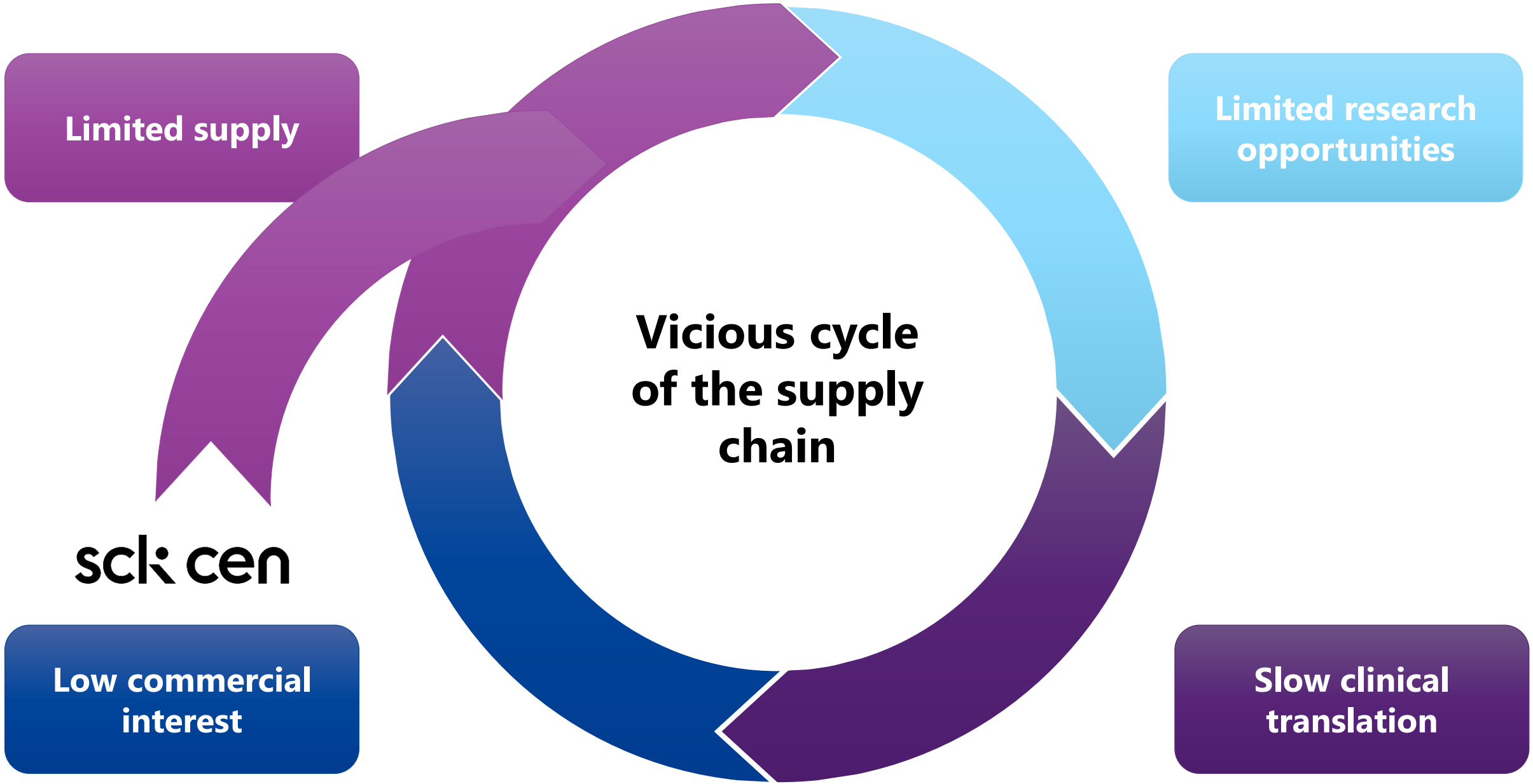
Limited supply

Limited research opportunities



Low commercial interest

Slow clinical translation


Limited supply
Limited research opportunities
Vicious cycle of the supply chain
Low commercial interest
Slow clinical translation

Thank you for your attention

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