

Targeting LAT1 with technetium(I)-99m-labeled tryptophan derivatives for SPECT imaging

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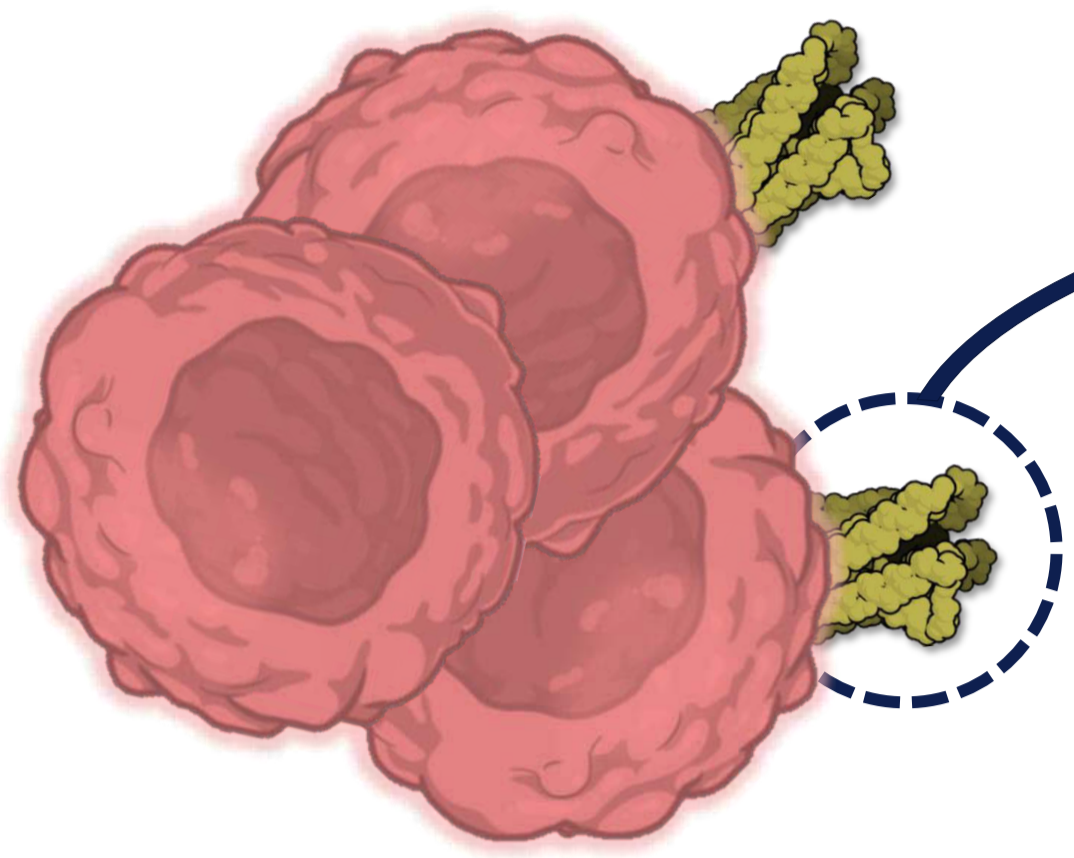
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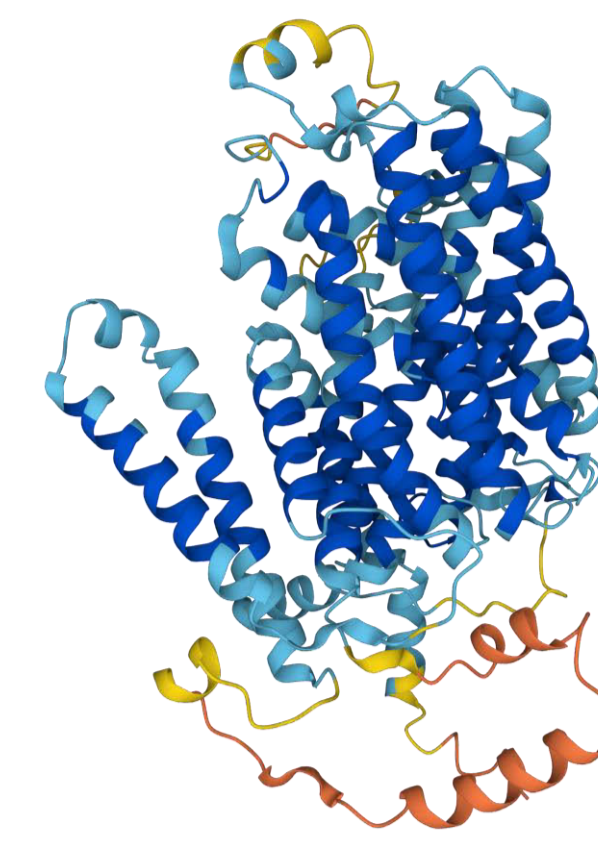
<https://doi.org/10.17952/37EPS.2024.P2017>

Cancer

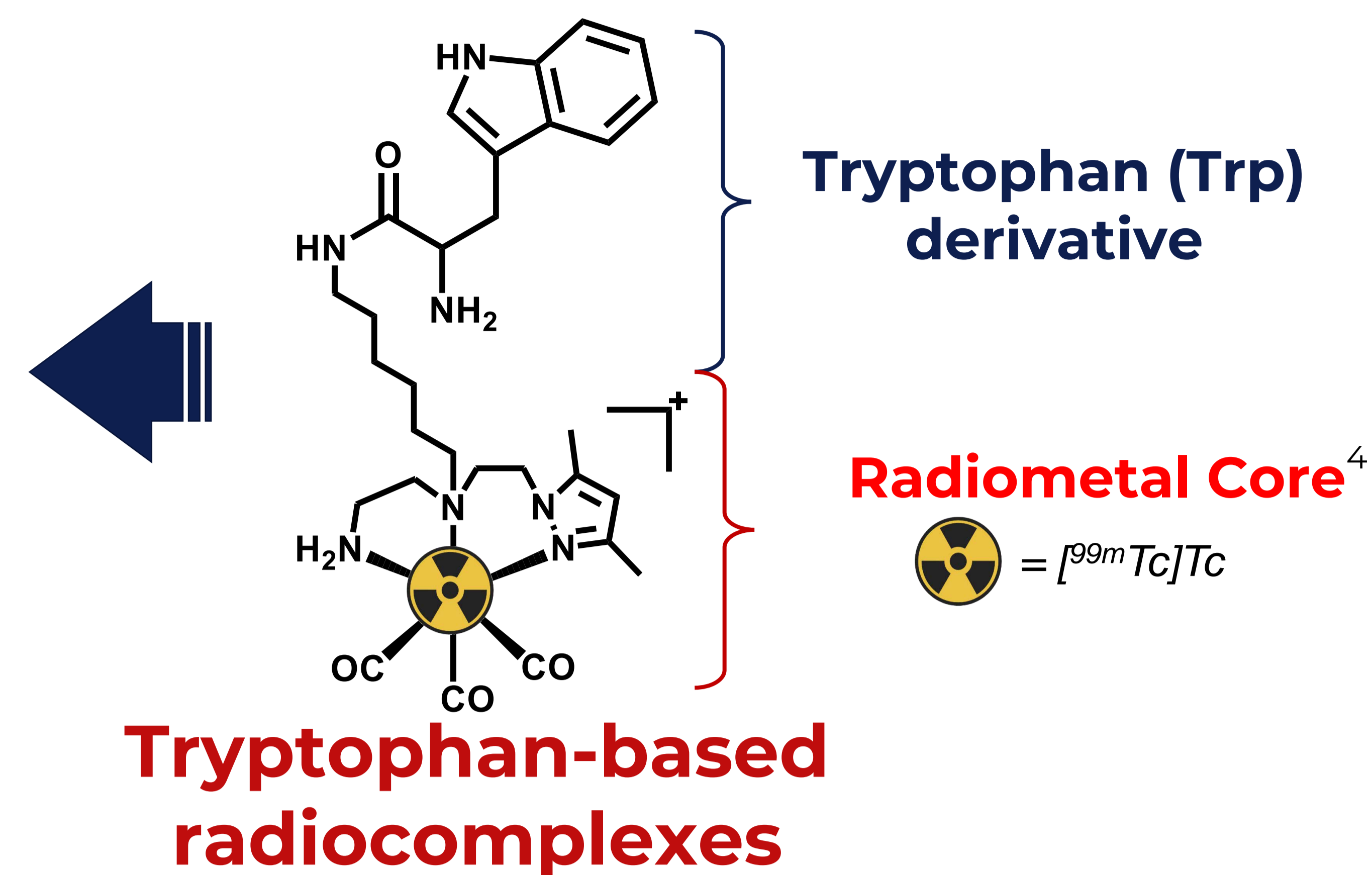


- UNCONTROLLED and UNLIMITED proliferation and growth are benchmark characteristics of cancer¹
- Metabolic reprogramming leads to an increase in nutritional needs of the cell²

Large Amino acid Transporter 1 (LAT 1)

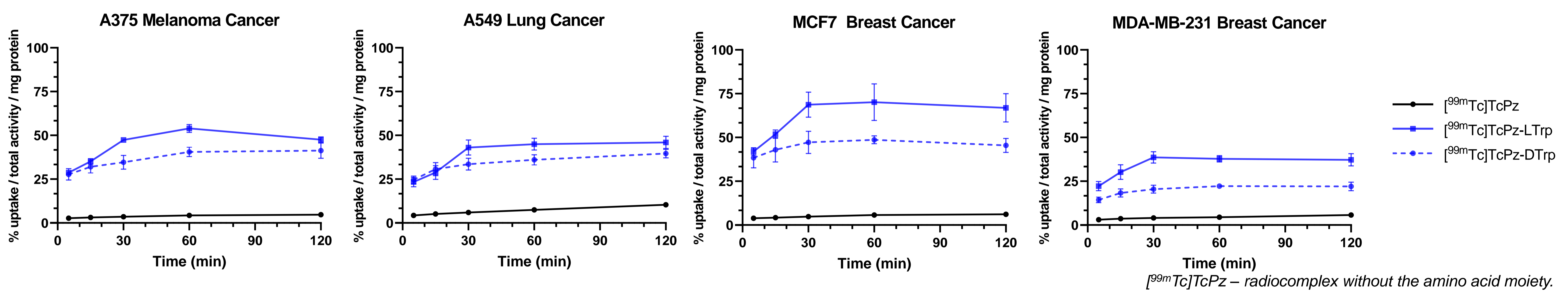


- LAT1 belongs to the solute carrier 7 family and is overexpressed in many types of cancers, including some of the most common, such as prostate, breast and lung cancer³
- LAT1 has been increasingly explored as a drug target for imaging and therapy of cancers

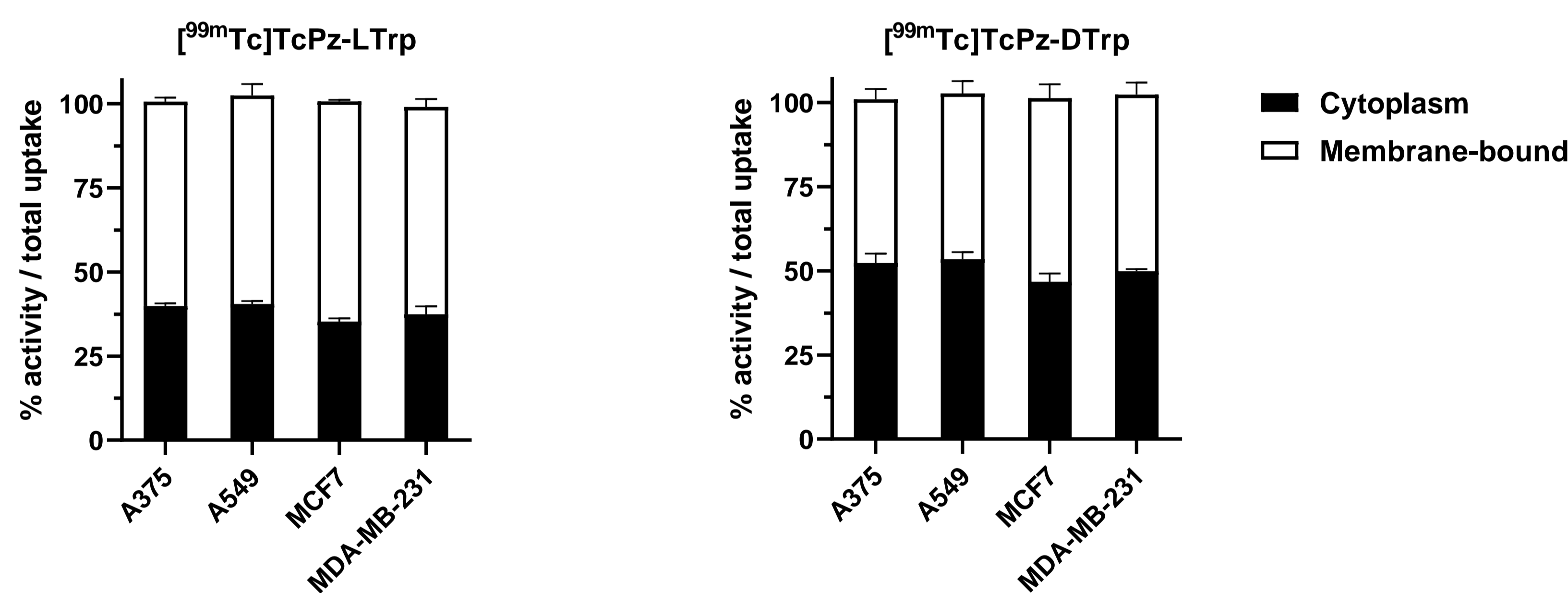
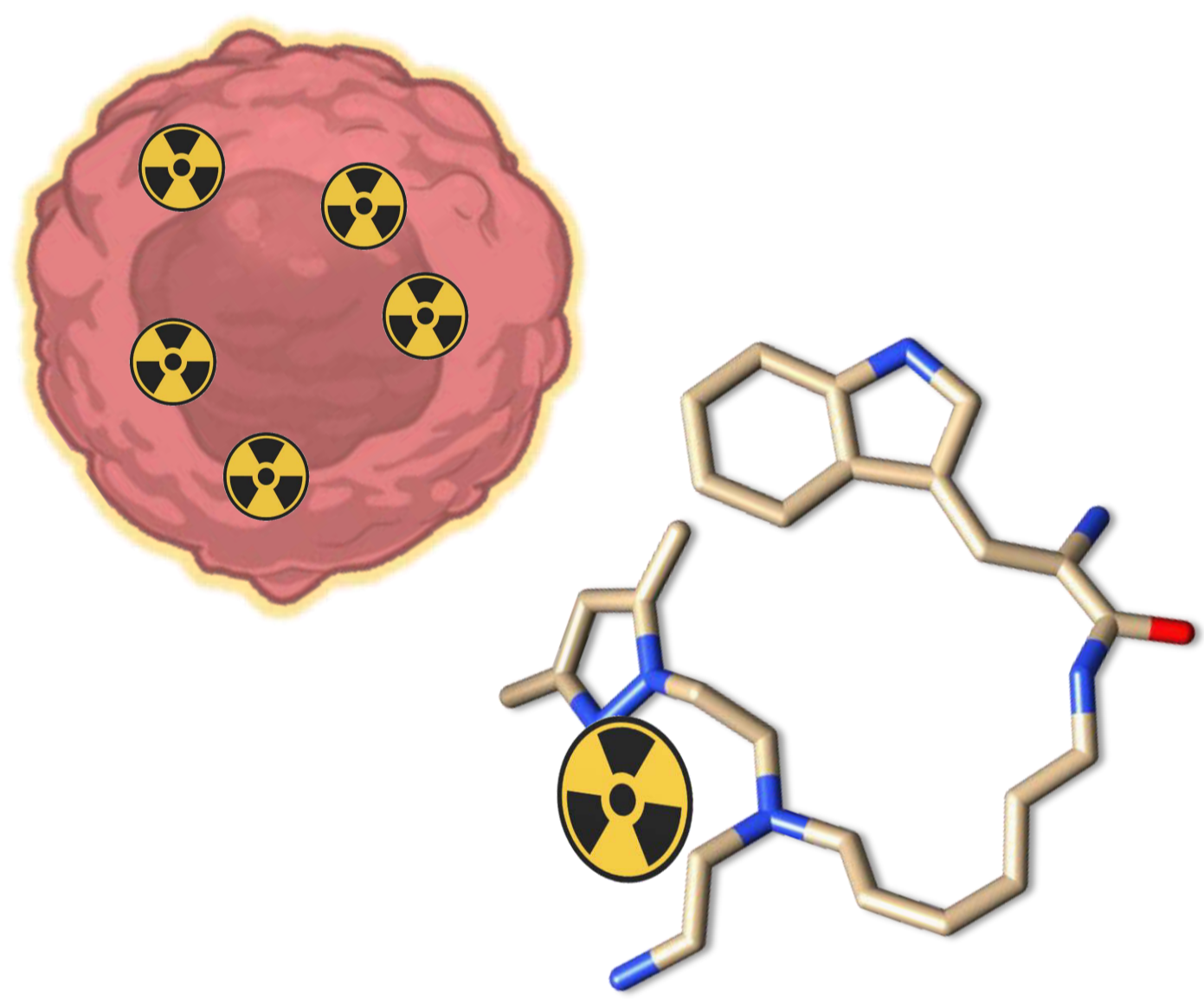


Trp-based radiocomplexes of the type *fac*-[^{99m}Tc(CO)₃(k³-Pz-Trp)]⁺ for targeting LAT1: Design and biological evaluation of potential tools for non-invasive cancer imaging

Cellular uptake of [^{99m}Tc]Tc-complexes based on the L/D-enantiomers of Trp



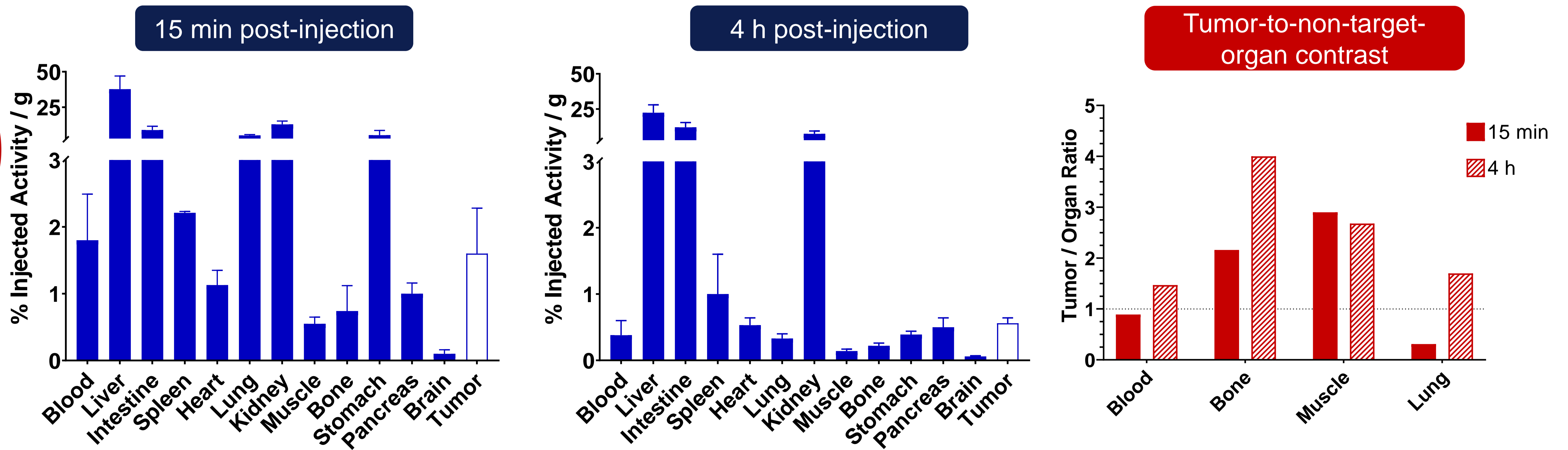
Cellular internalization



40 to 50% of the total cell-related activity is found intracellularly

Biodistribution studies of [^{99m}Tc]TcPz-LTrp in mice bearing A549 lung cancer xenografts

[^{99m}Tc]TcPz-LTrp presents tumor accumulation but poor contrast



Conclusions

- The cellular uptake depends on the enantiomeric form of Trp, with the L-Trp-bearing radiocomplex presenting the highest values.
- MCF7 breast cancer cell line shows the highest overall uptake.
- 40 to 50% of the total cell-related activity is found intracellularly.
- [^{99m}Tc]TcPz-LTrp shows fast tumor uptake in tumor-bearing mice but poor tumor-to-non-target organs contrast.

References:

- Vaupel et al., *J. Physiol.* **2021** 599(6),1745
- Yasuhiro et al. *Cancer Sci.* **2021** 112(8), 2958
- Wei et al. *Front. Cell Dev. Biol.* **2021**, 8, 603837
- Morais et al., *Dalton Trans.* **2017**, 46, 14537

