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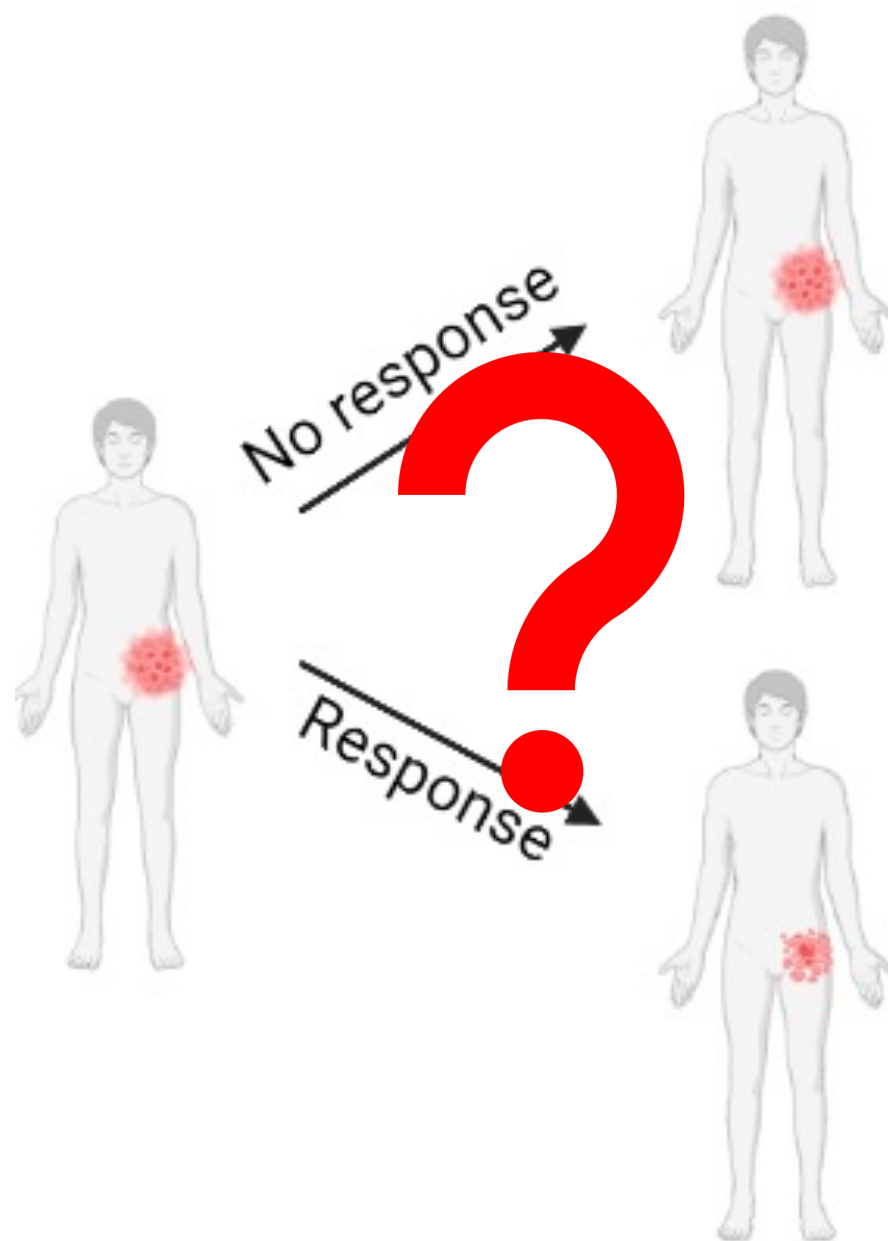
Synthesis and assessment of a novel, carbohydrate-derived caspase-3 radiotracer

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Introduction



RECIST

- Morphological changes
- Late biomarker
 - Pseudoprogression



Cell death

- Early event
- Undisputable biomarker

➤ Cell death as an early biomarker for treatment response.

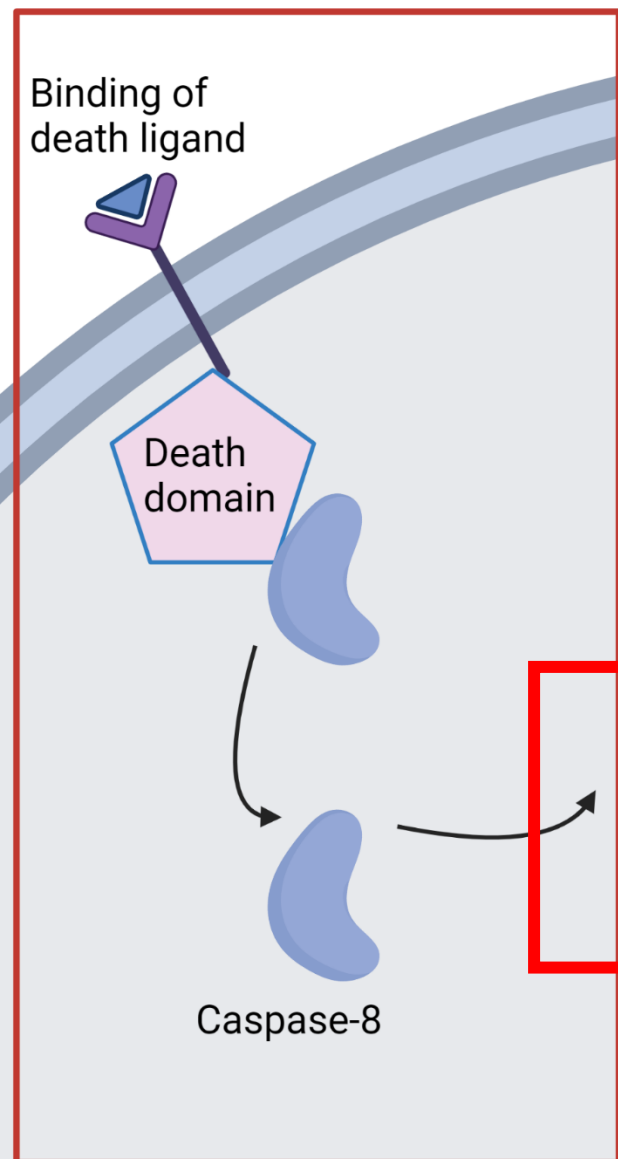
PET imaging

- Non-invasive measurement
- Heterogeneity of tumours
- High spatial resolution

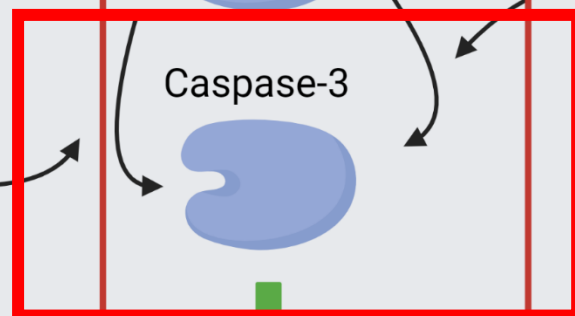
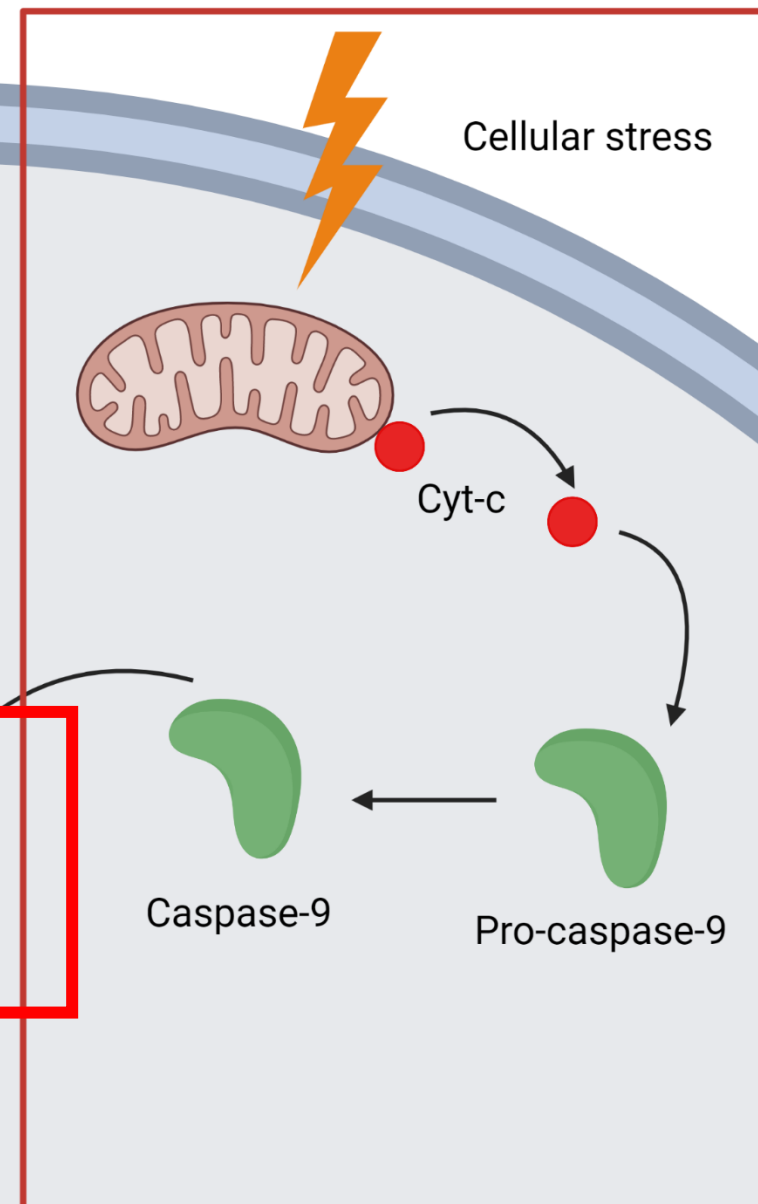


Apoptosis imaging

Extrinsic pathway



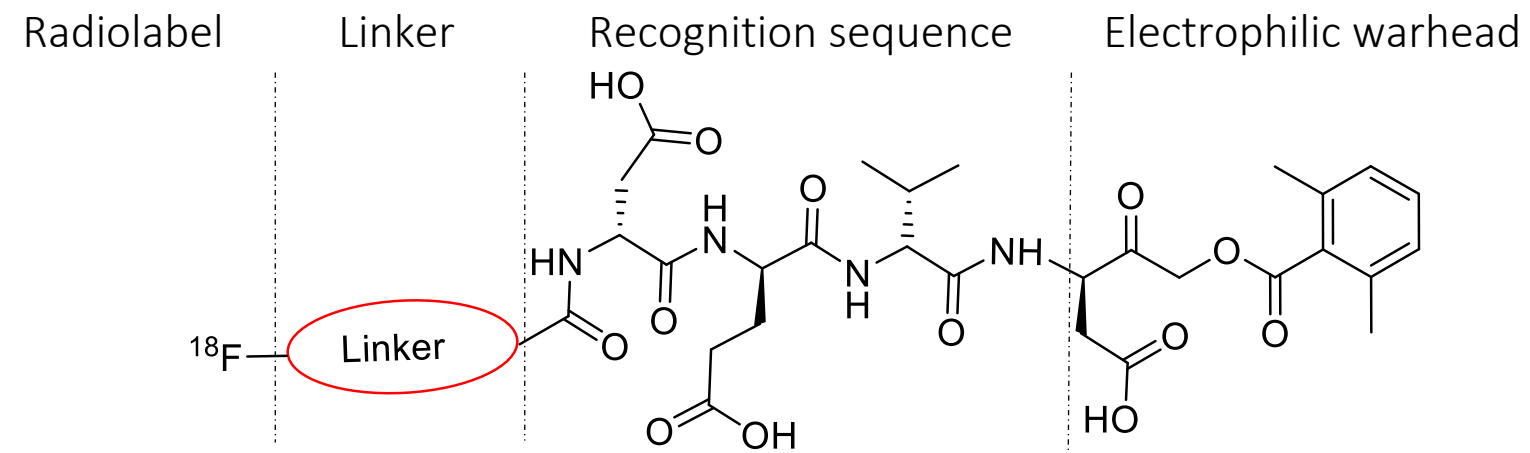
Intrinsic pathway



Apoptosis

Methods

1st generation
DEVD-based probes



1st generation

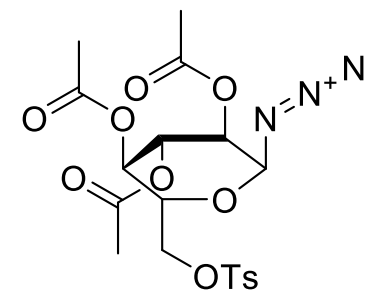
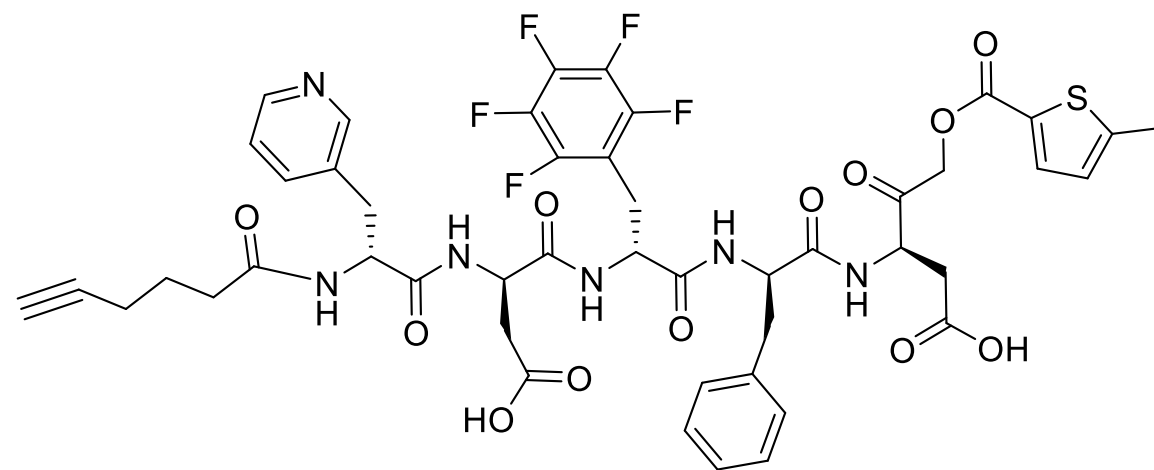
- Fast binding kinetics
- Low Caspase-3 selectivity



Methods

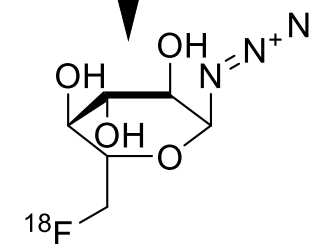
Small library of ABPs targeting caspase-3

- ❖ Increased hydrophilicity by linker modification
- Increased renal clearance
- Higher tumour-to-background ratio



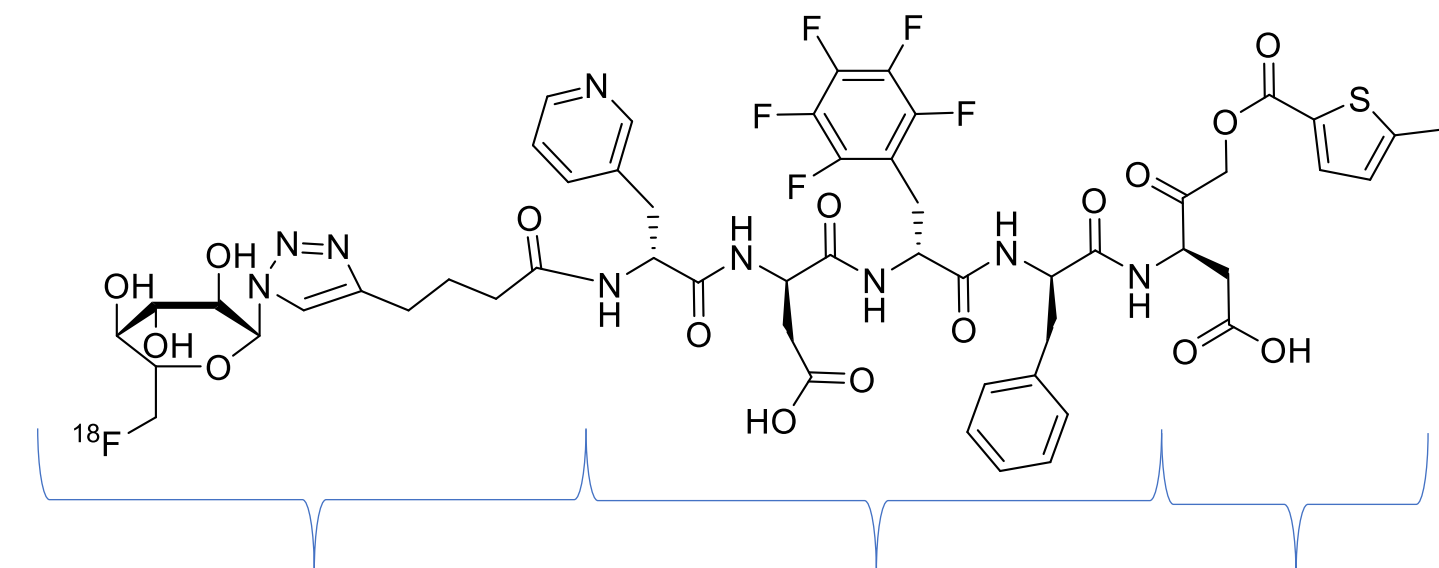
1 $[^{18}\text{F}]\text{F}^-$, TEAB, MeCN, 100°C, 10 min

2 NaOH, RT, 2 min



CuSO₄, sodium ascorbate, THPTA
20 minutes, RT

$[^{18}\text{F}]\text{MICA-320}$



Tag and linker

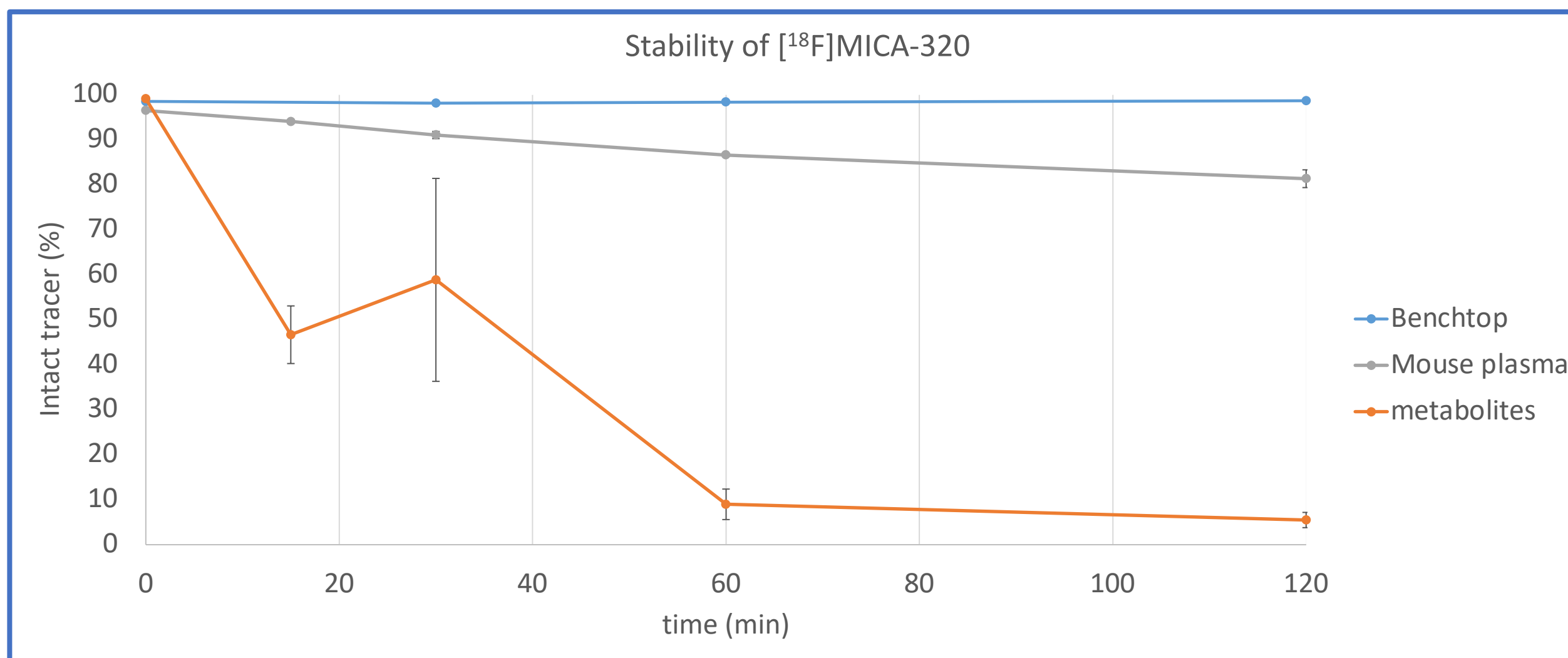
Recognition
Sequence

Warhead



Results

RCY (%) (N=3)	RCP (%) (N=3)	Molar activity (GBq/ μ mol) (N=3)	LogD (N=3)
7.9 $\pm$ 4.4	98.9 $\pm$ 0.23	333 $\pm$ 225	-1.20 $\pm$ 0.19

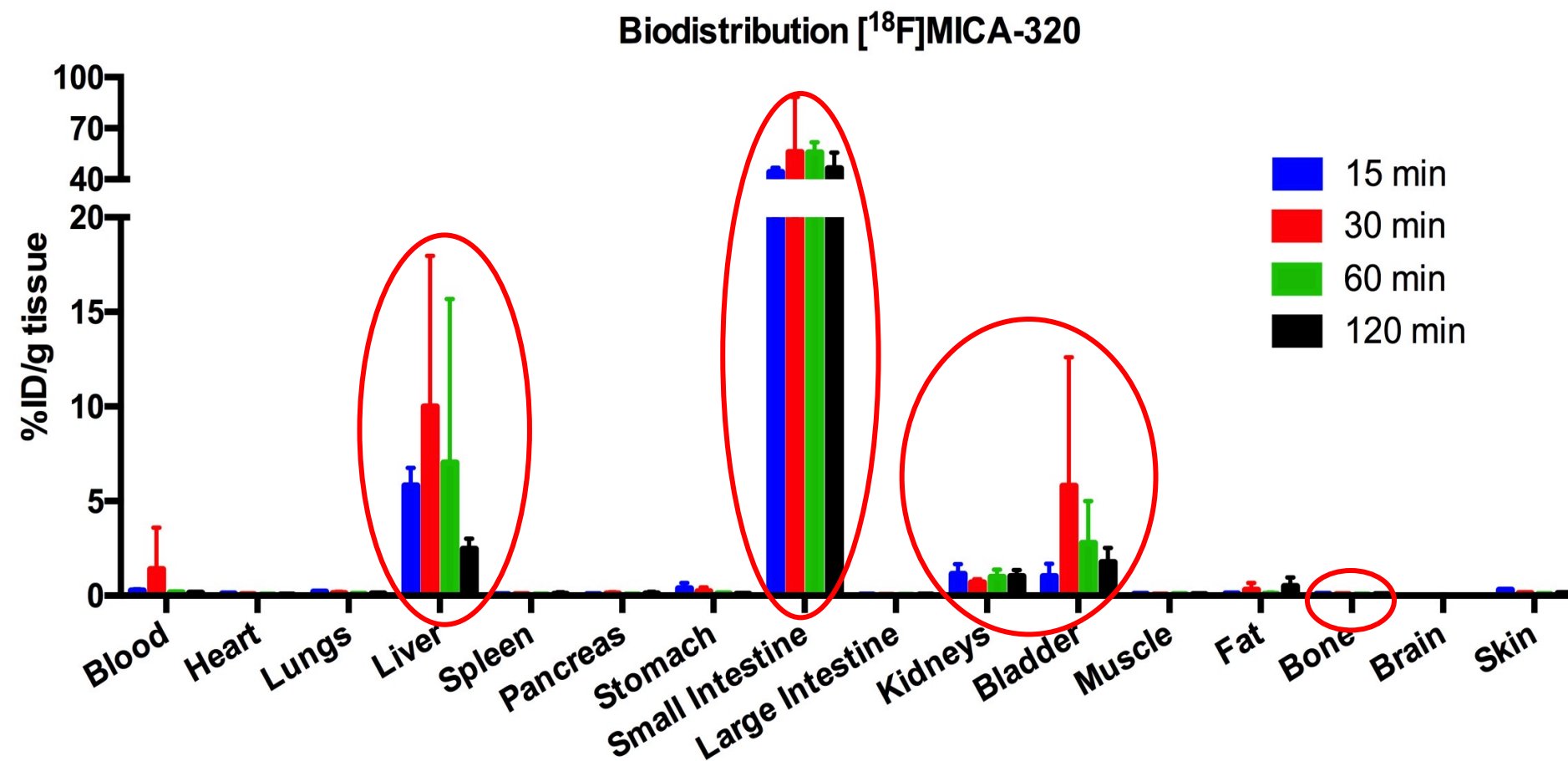


- Formulation, RT (N=1)
- Mouse plasma, 37°C (N=3)
- CD-1 nude mice (N=3)



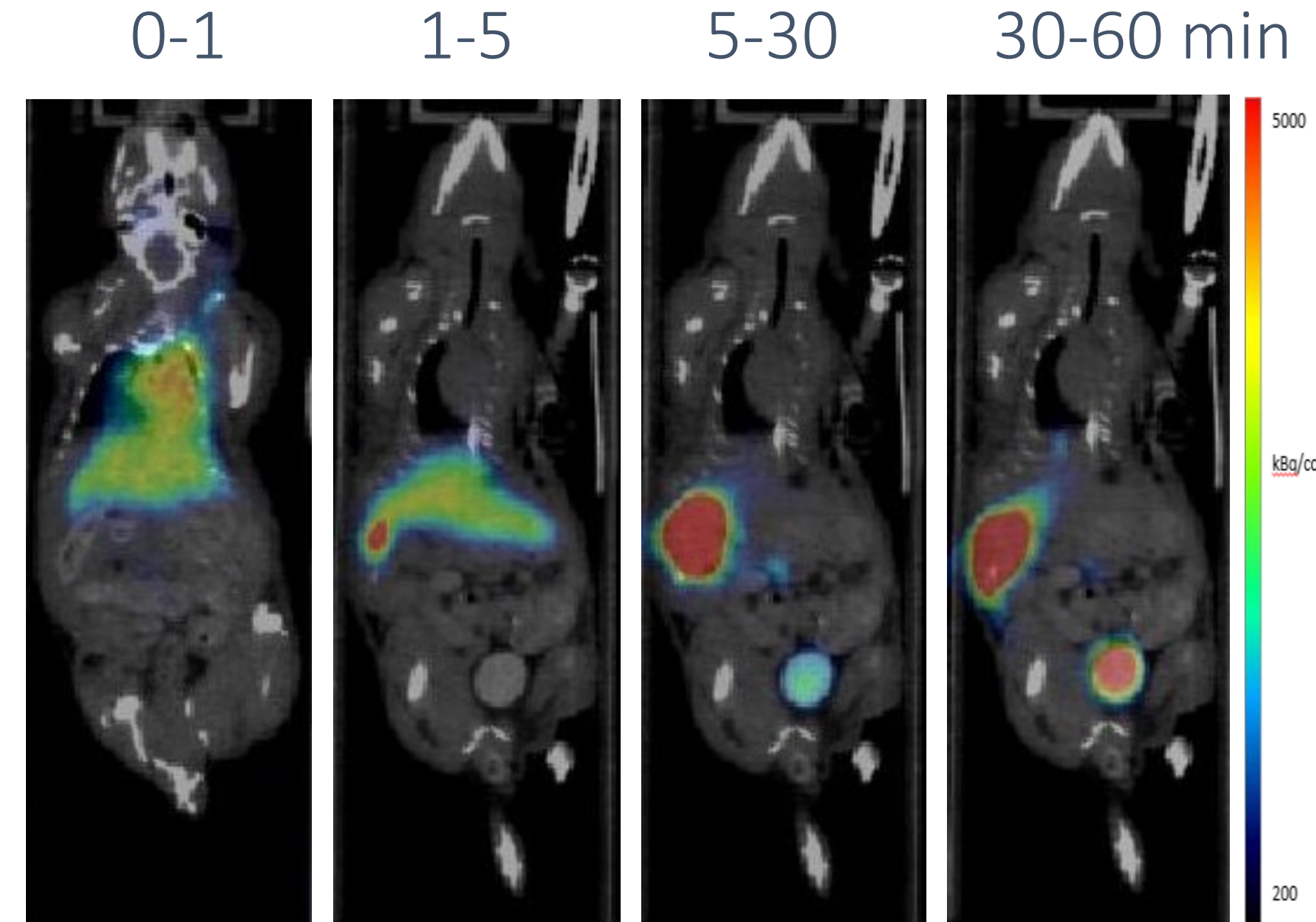
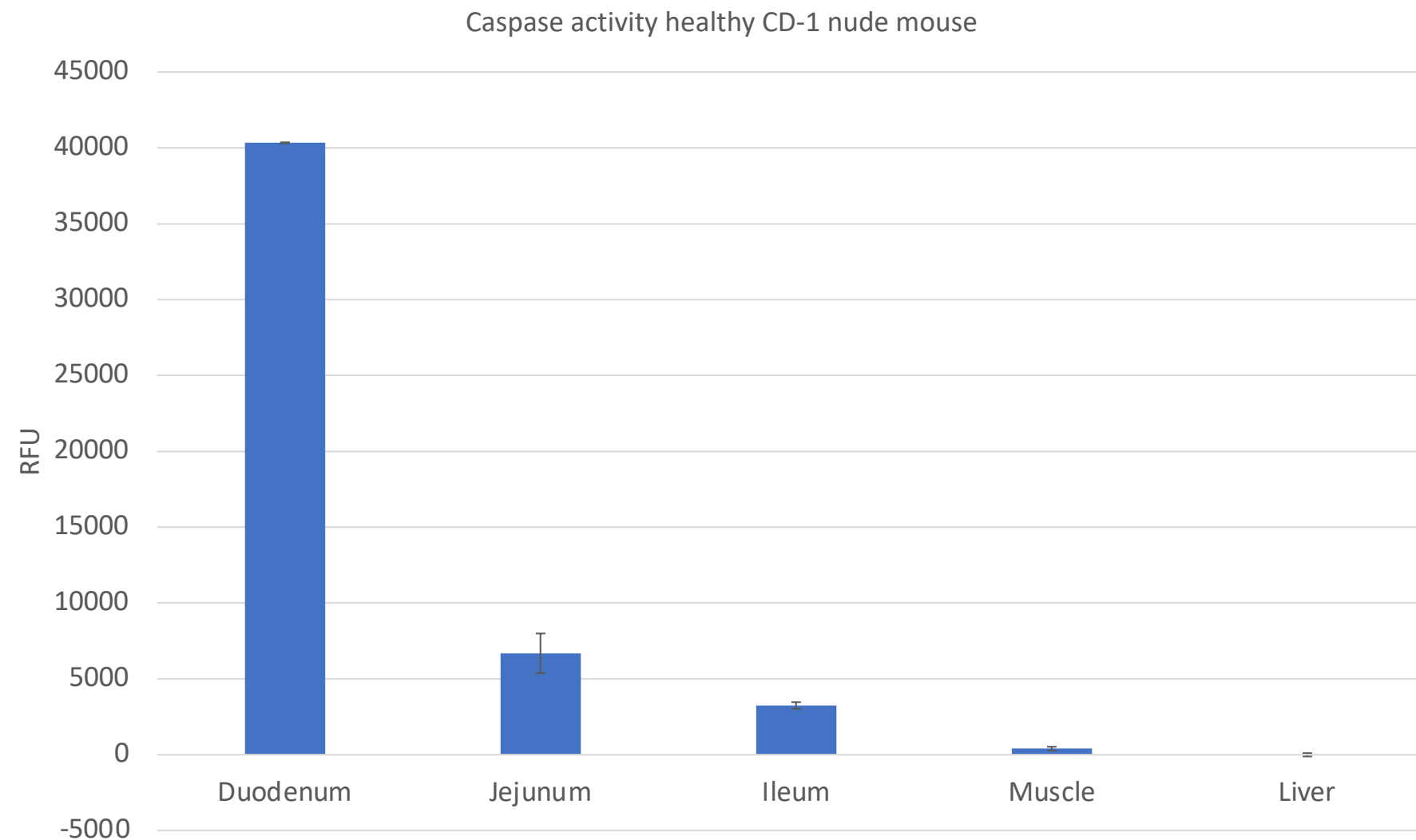
Results

- Biodistribution assessed in CD-1 nude mice (N=3/timepoint)



Results

Caspase-3 activity was measured in the small intestine of a CD-1 nude mouse.



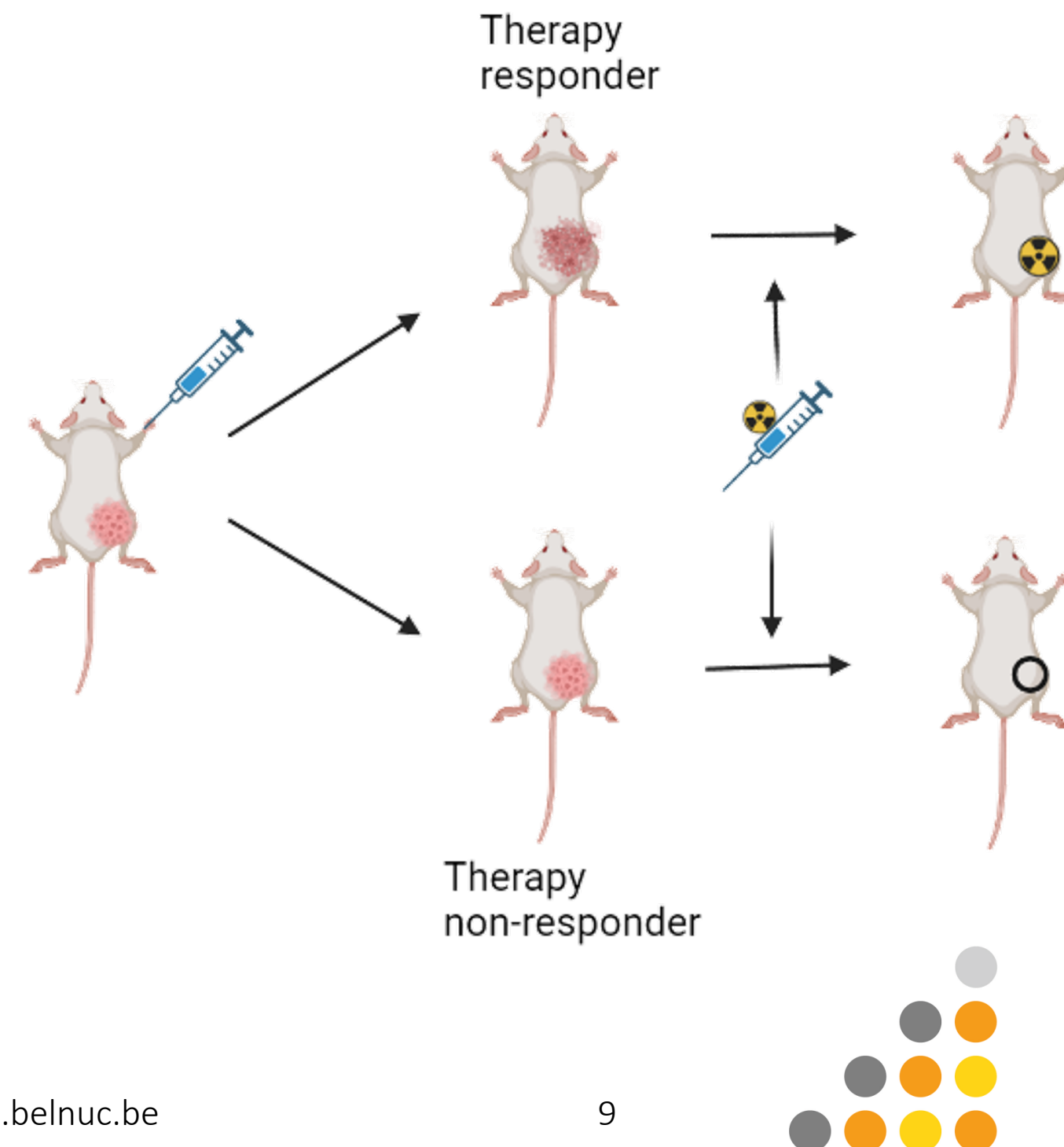
Conclusions & future perspectives

Preliminary data warrants further preclinical investigation:

- Adequate yield and high molar activity
- Lack of *in vivo* defluorination and adequate stability
- Mixed renal/hepatobiliary clearance

Further characterisation

- Assessing *in vitro* binding capability
- Evaluating early tumour response in a human cancer xenograft treated with immunotherapy



Acknowledgements

