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Society for Immunotherapy of Cancer



Flexible ^{64}Cu -nanoparticle-based cell labeling system allows for *in vivo* tracking of adoptively transferred T-cells by PET/CT

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Presenting: **Hólmfríður Rósa Halldórsdóttir M.Sc.**
Technical University of Denmark

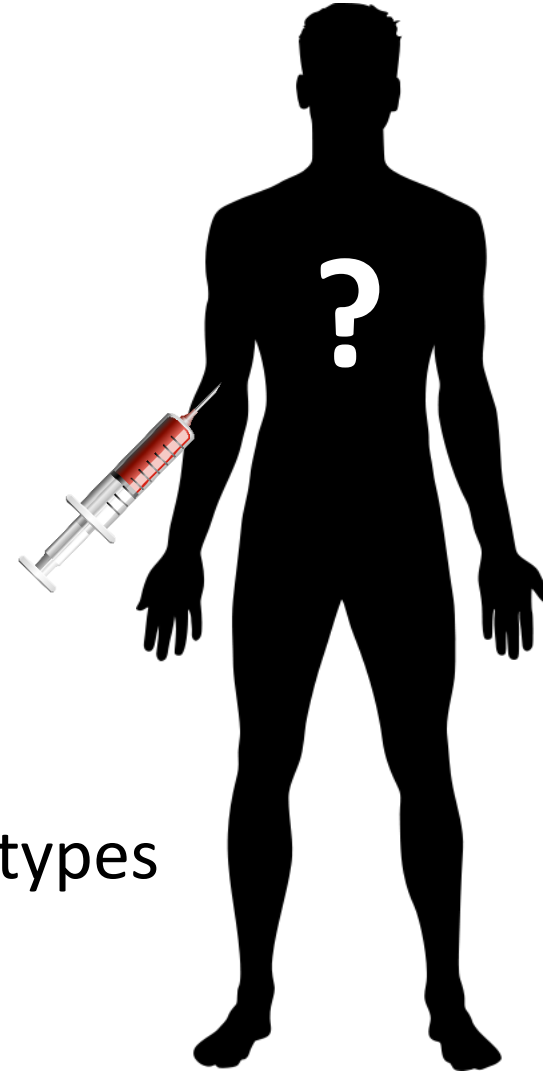


Financial relationships

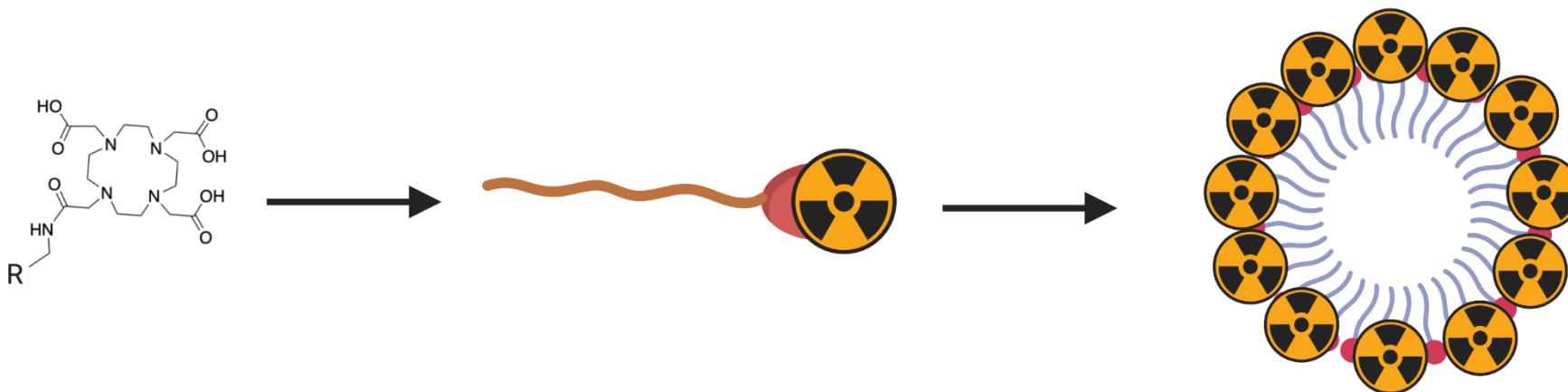
Nothing to disclose

Why is this of value?

- Adoptive cell transfer
 - Where do the cells go?
 - When do they reach the tumor?
 - Timing of adjuvant therapy!
- Real time tracking
- Flexible system: Labelling of different cell types

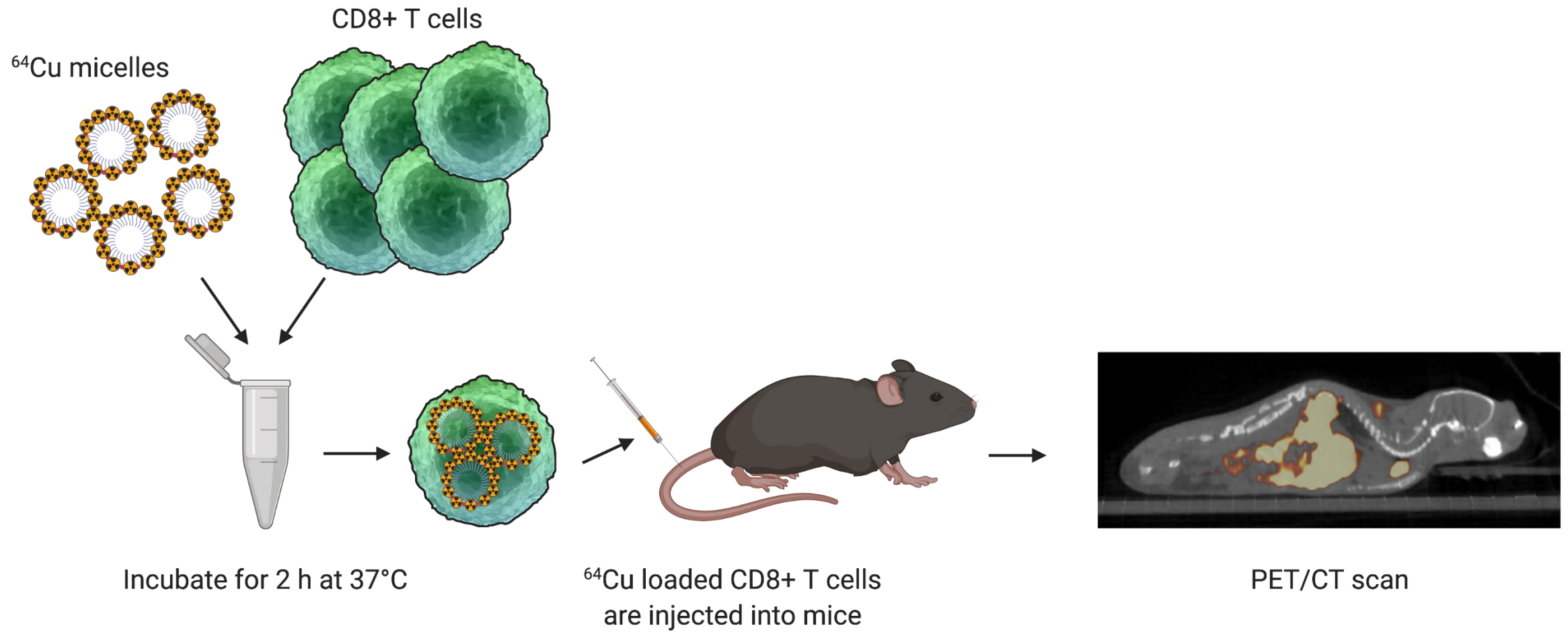


The flexible ^{64}Cu -nanoparticle-based cell labeling system



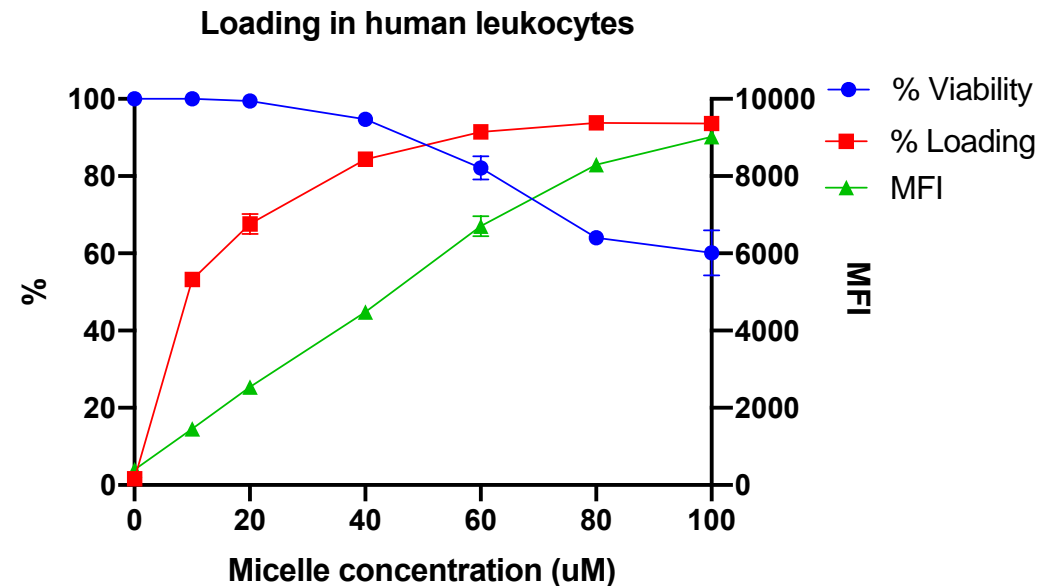
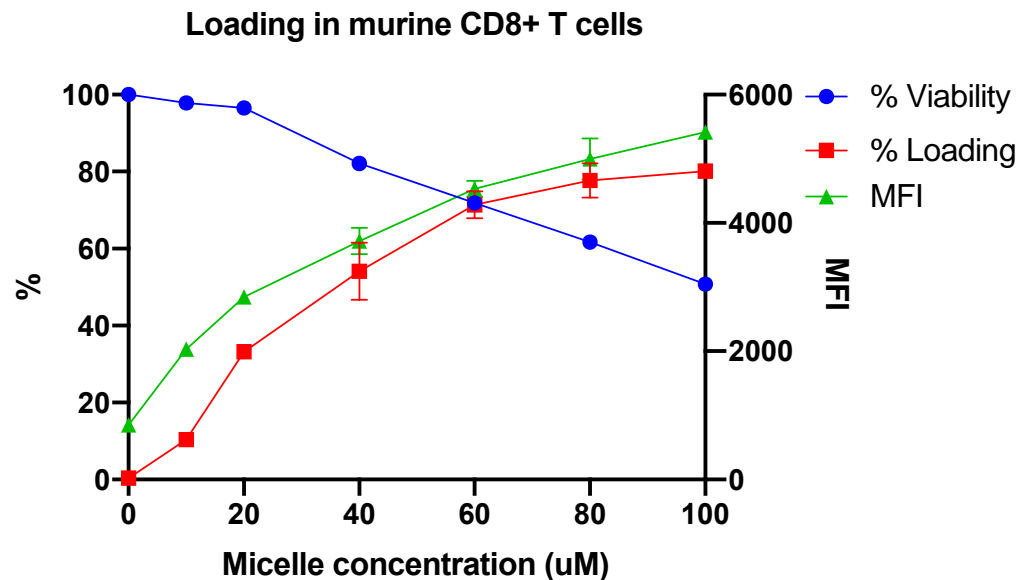
- Micelle formulation with a DOTA chelator.
- Flexible radiolabeling.
- Provides high specific radioactivity.

Protocol

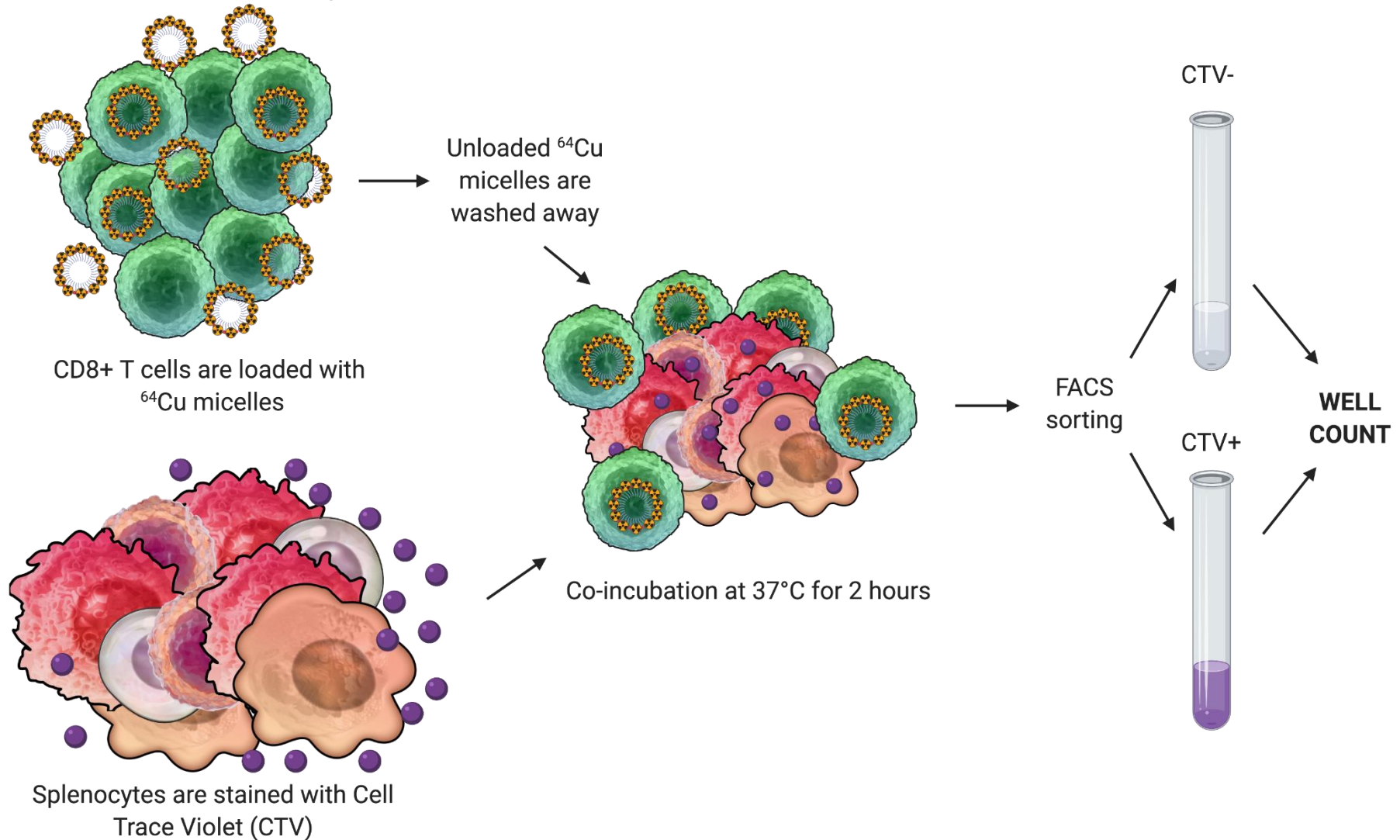


Loading parameters

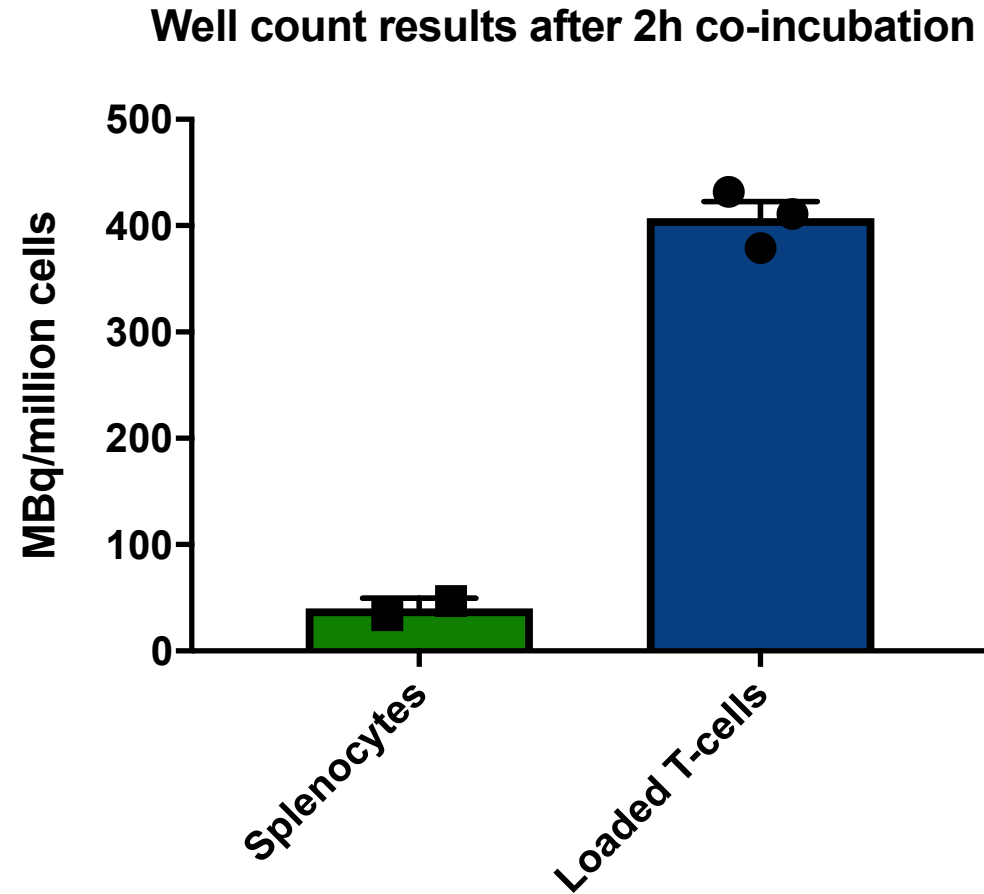
For optimizing the loading protocol we incorporated a fluorophore into our micelle construct.



Micelles are stably retained within loaded T cells



Micelles are stably retained within loaded T cells

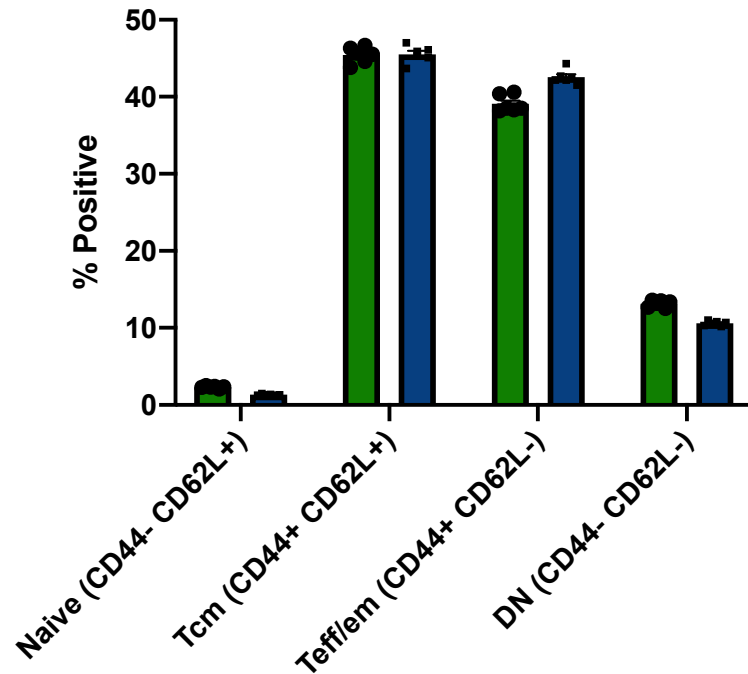


Mean \pm SEM

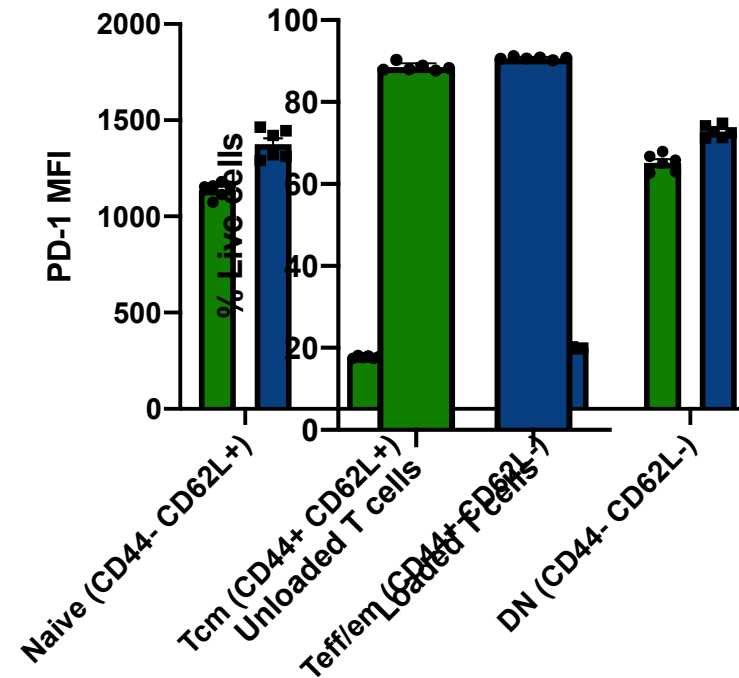
Data by Lars Ringgaard

Micelle loading does not change T cell phenotype

CD8+ T cell phenotype 3 days after loading



Viability after 3 days



■ Unloaded T cells
■ Loaded T cells

Mean ± SEM

Proof of concept *in vivo*

How do we prove it is the loaded T cells we see in the PET/CT scans?

Proof of concept *in vivo*

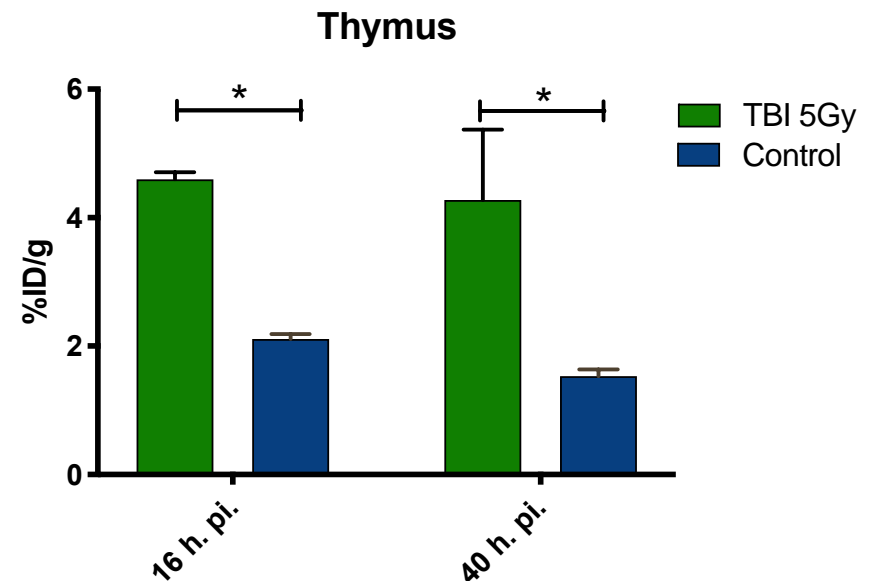
How do we prove it is the loaded T cells we see in the PET/CT scans?

Journal of experimental medicine 1991:

Reentry of T Cells to the Adult Thymus Is Restricted to Activated T Cells

By David B. Agus, Charles D. Surh, and Jonathan Sprent

*From the Department of Immunology, Research Institute of Scripps Clinic,
La Jolla, California 92037*

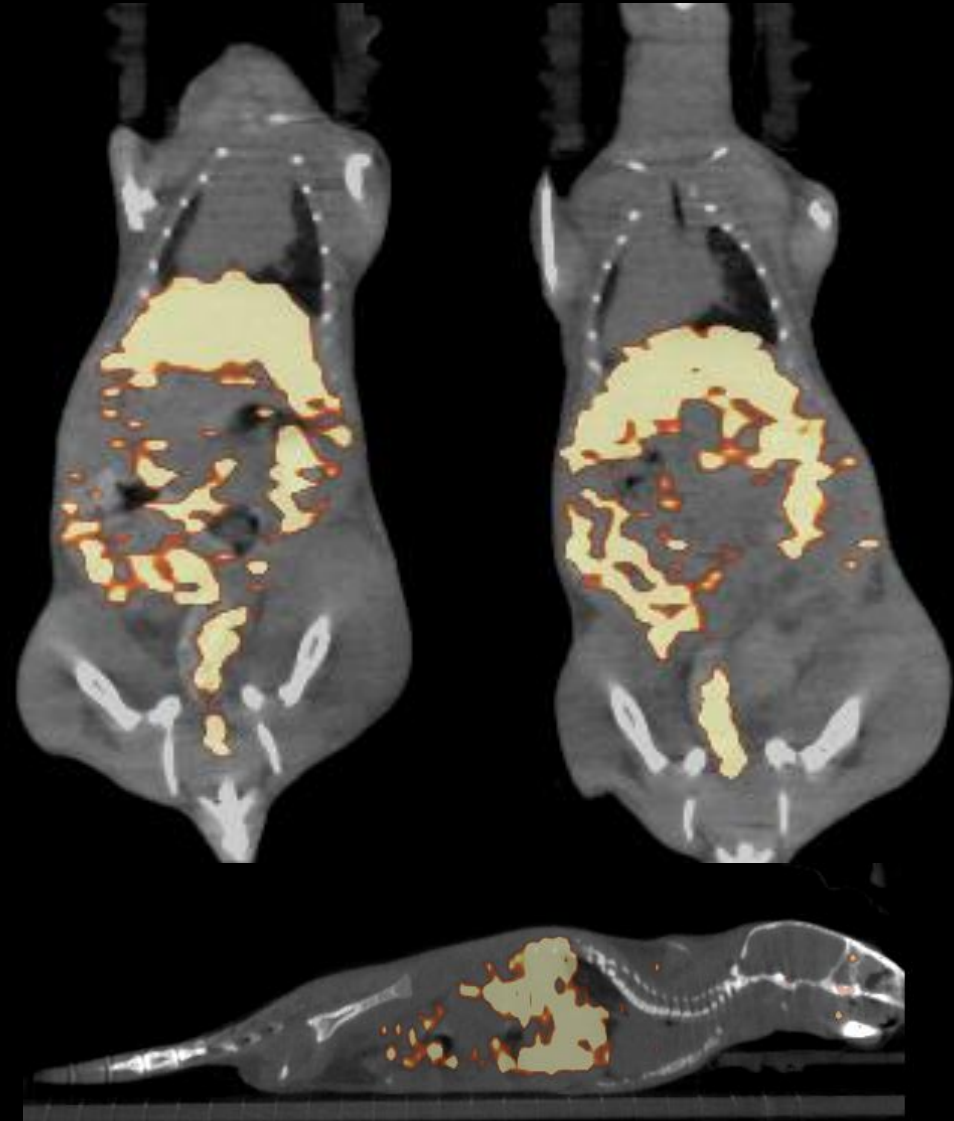
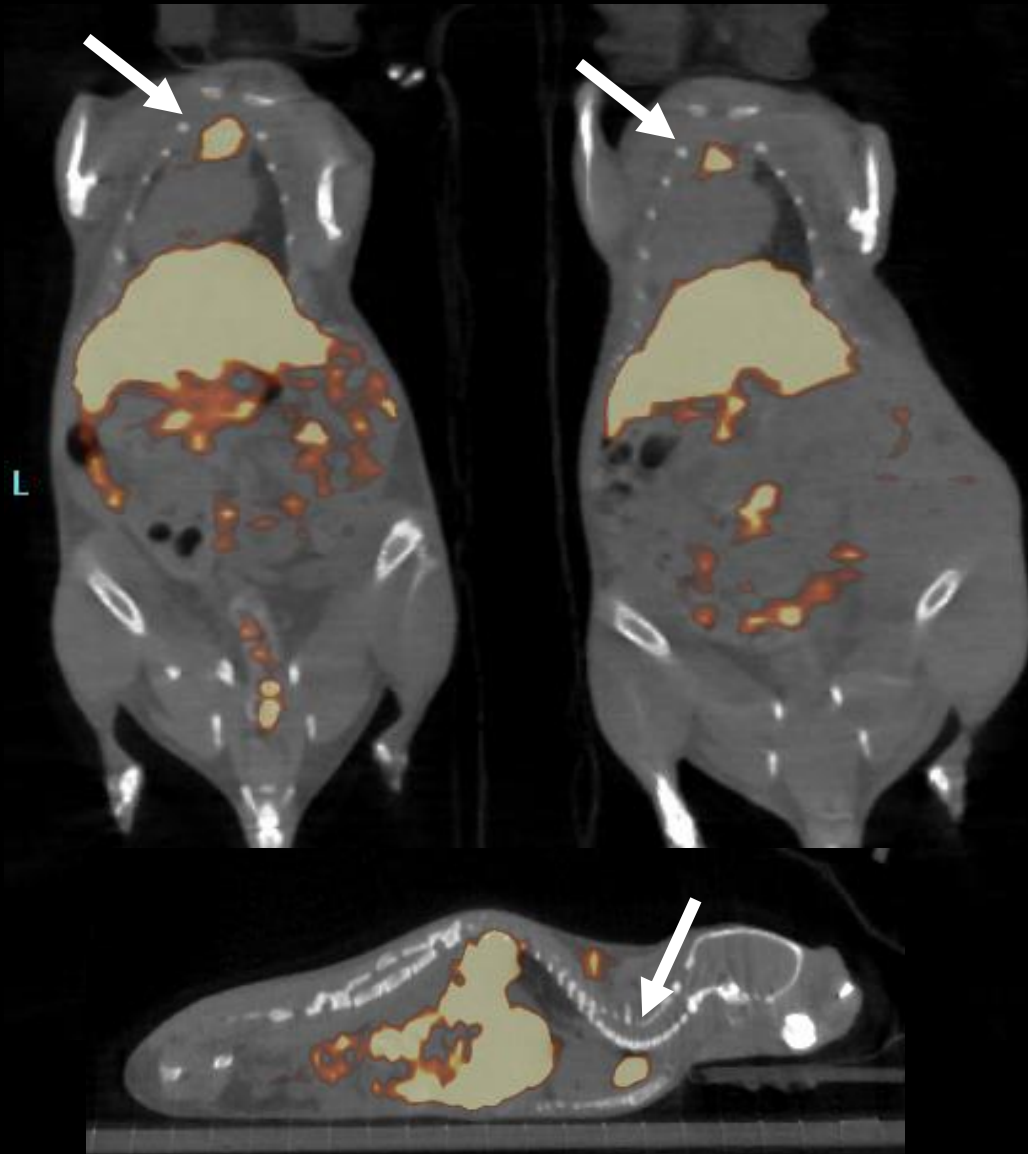


Total body irradiated mice

48 hours after injection

Loaded T cells

Free micelles



Data by Lars Ringgaard and Ditte Jæhger

Radioactivity follows T cell numbers

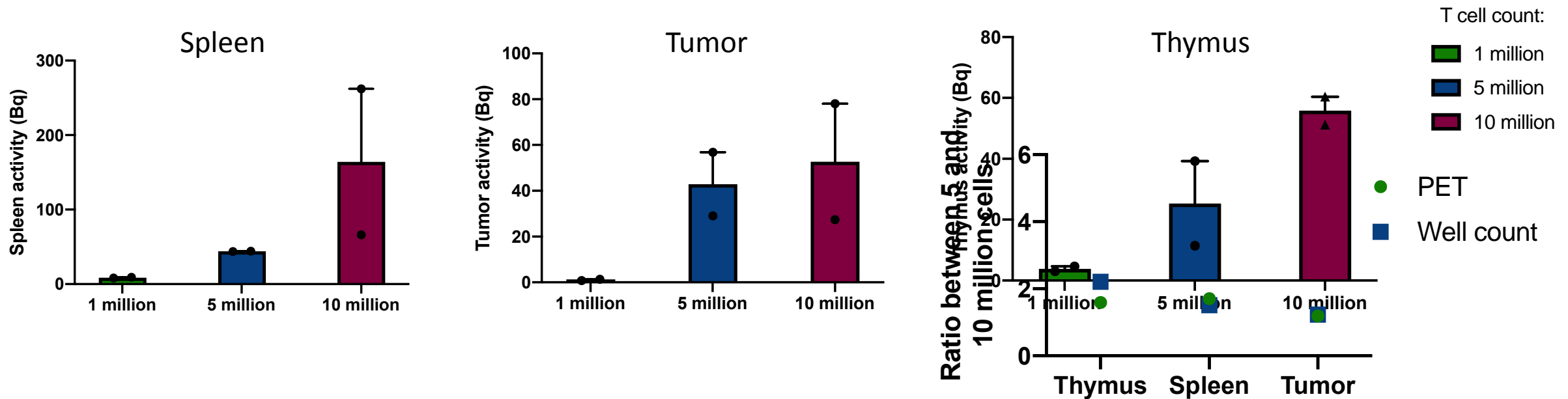
Mice were injected with 1, 5 or 10 million loaded T cells.

Radioactivity was measured after 24 h in spleen, thymus and tumor using PET/CT.

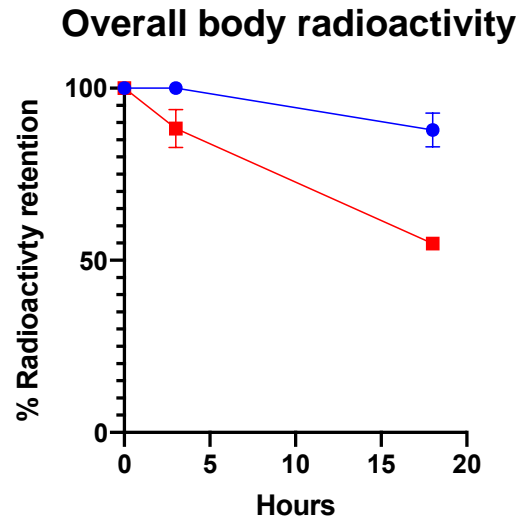
Organs were then harvested and radioactivity in the organs was measured using a well counter.

Radioactivity follows T cell numbers

Well count data:



T cell biodistribution

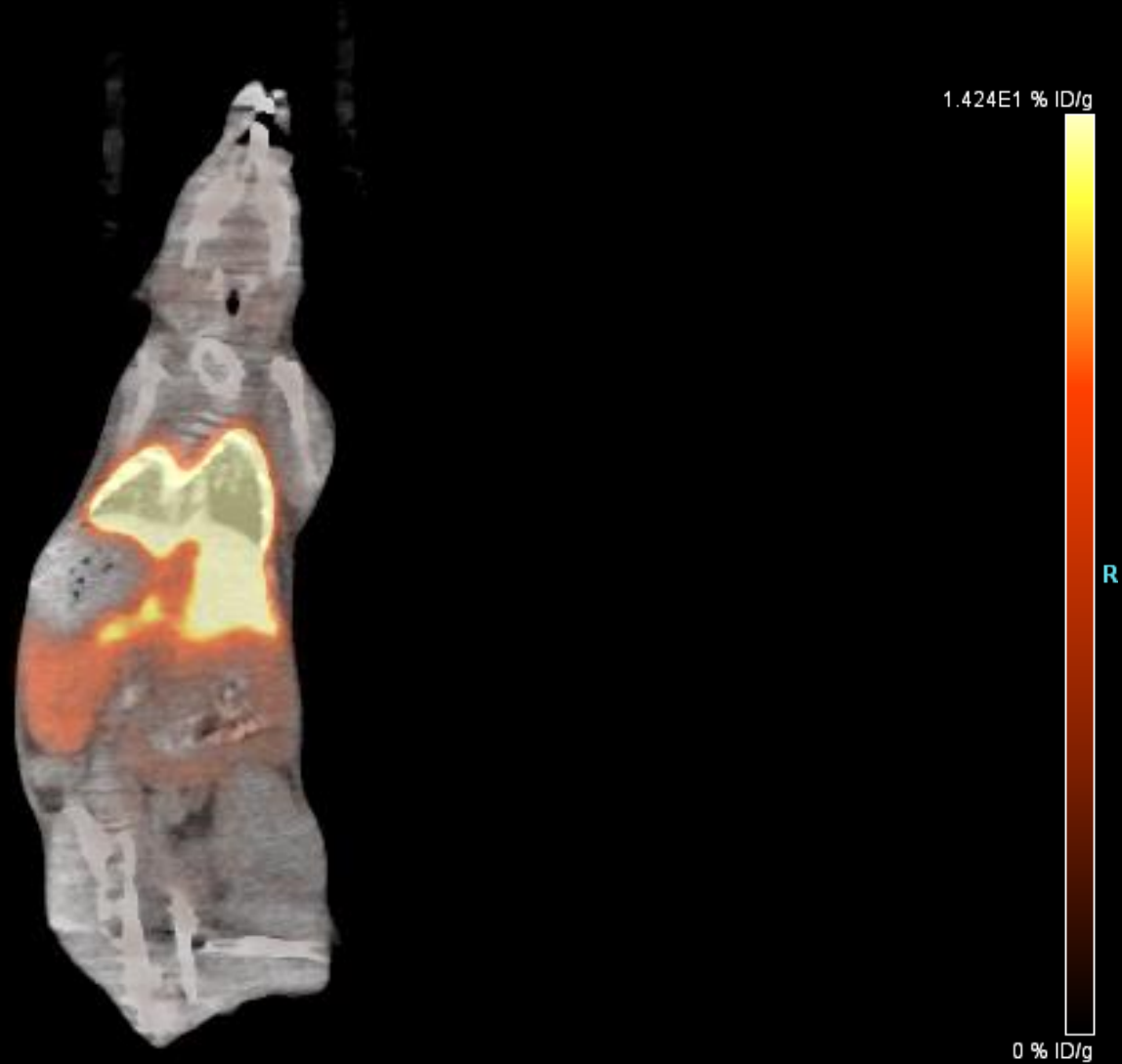


● Loaded T cells
■ Free micelles

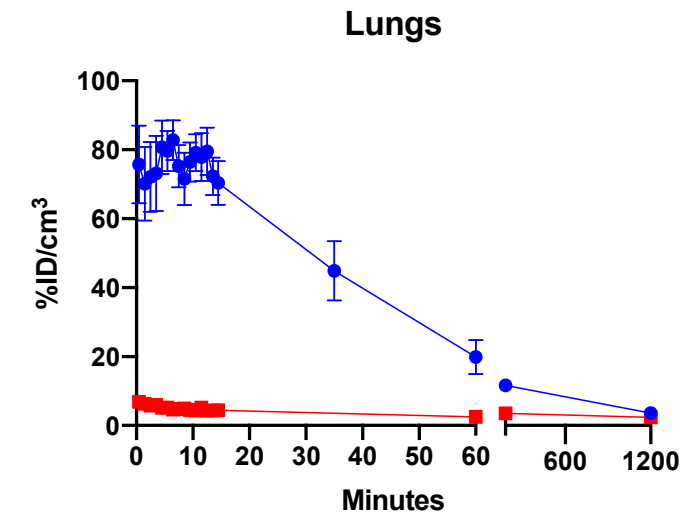
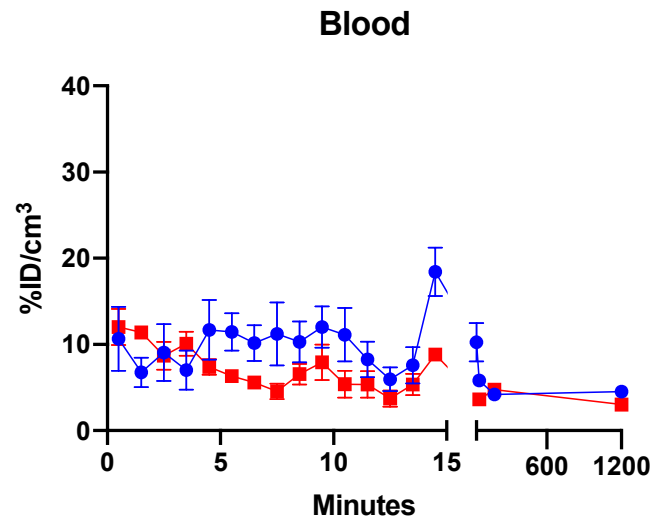
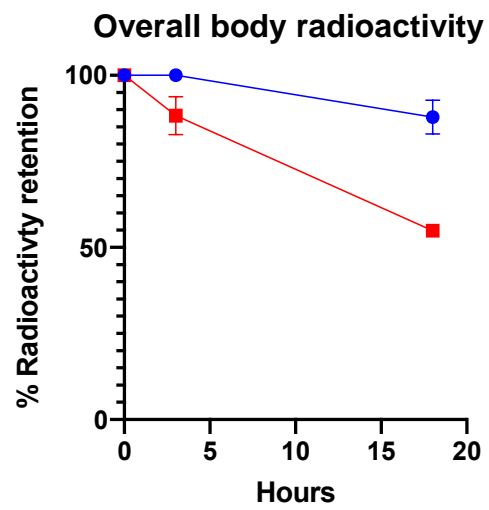
n=6
Mean \pm SEM

Loaded T cells home to lungs

Immediately after injection



T cell biodistribution

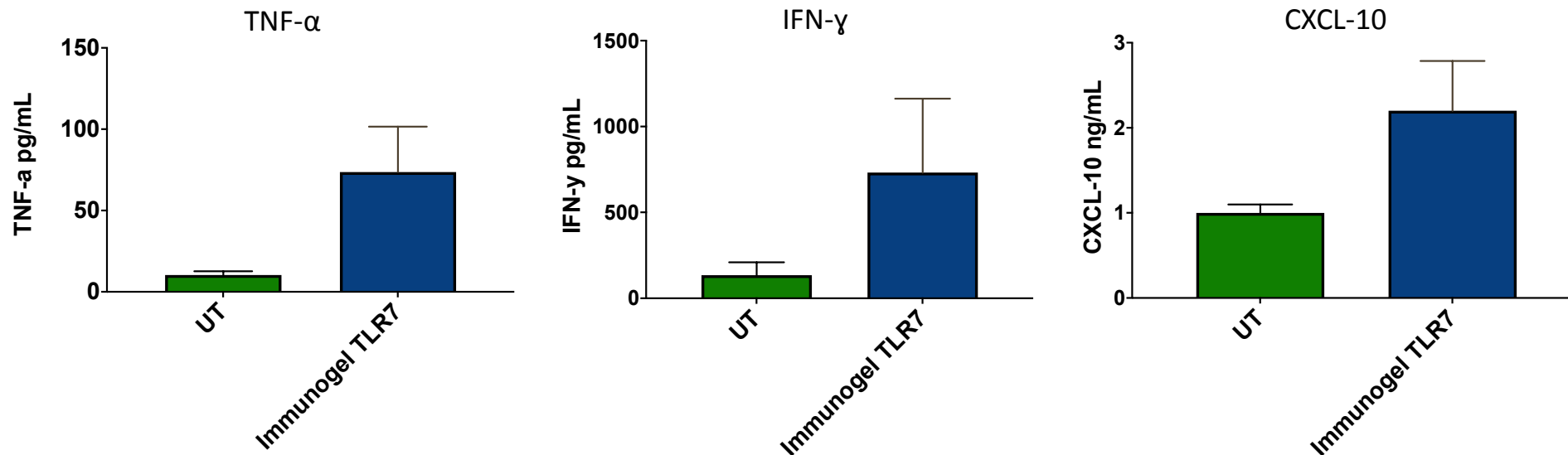


● Loaded T cells
■ Free micelles

n=6
Mean ± SEM

T cell theranostic imaging

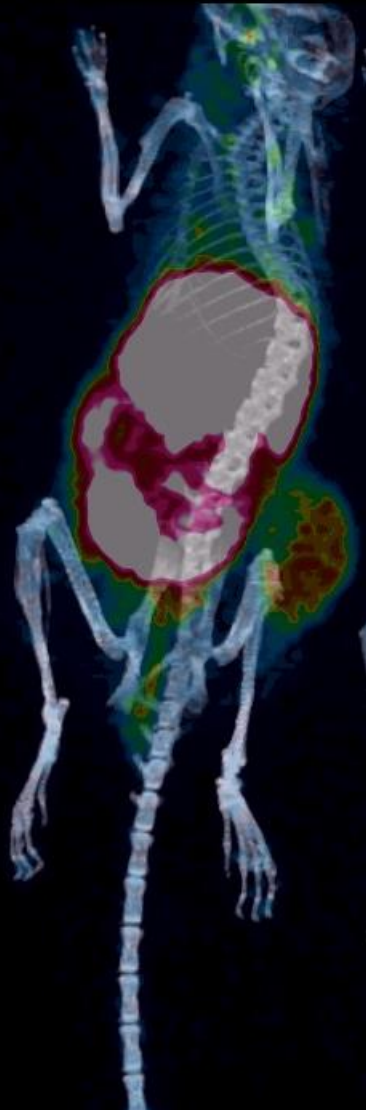
- Treated tumor bearing mice with i.t. Immunogel TLR7 agonist
- Immunogel TLR7 agonist increases intratumoral cytokine levels of T cell recruitment factors.
- Adoptive cell transfer with 10 million of ^{64}Cu -loaded T cells and scanned the mice after 40 h.



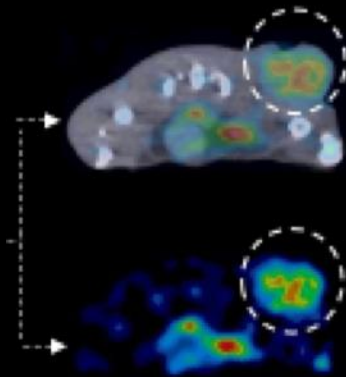
T cell infiltration into tumor when treated i.t. with Immunogel TLR7 agonist

Example of data 40 hours after adoptive cell transfer

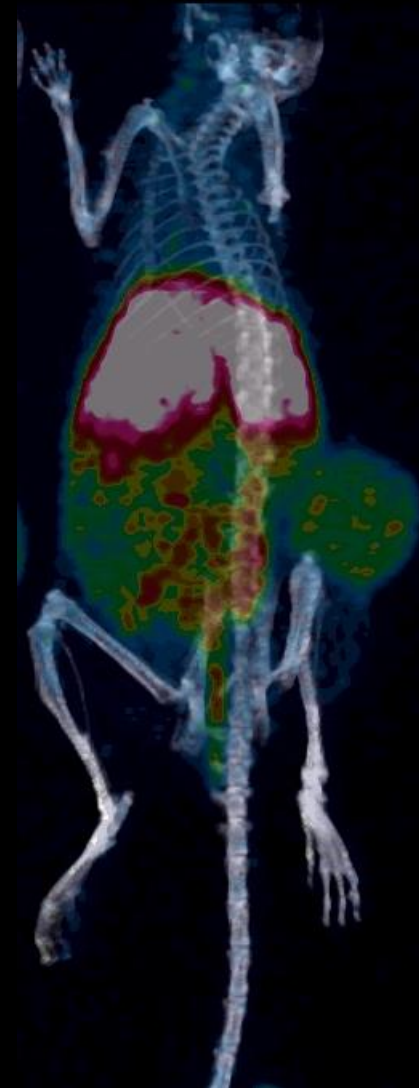
Treated with Immunogel TLR7



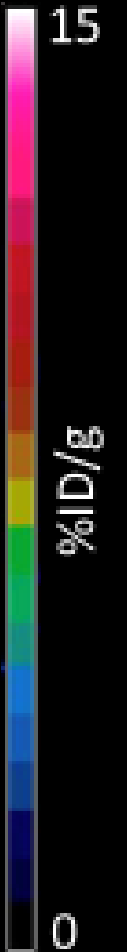
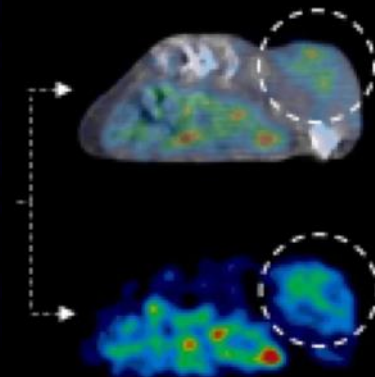
Tumor activity
Mean: 3.8%ID/g
Max: 11.8%ID/g



Untreated



Tumor activity
Mean: 2.8%ID/g
Max: 8.9%ID/g



Conclusions and perspectives

- Flexible immune cell labelling method for in vivo tracking
- Comparison of loaded immune cell infiltration across different treatments
- Dynamic imaging of T cell trafficking patterns allows for the informed timing of adjuvant therapy

Acknowledgements

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 - Andreas Kjær
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-
- CBIO group at Technical University of Denmark
 - CMI group at University of Copenhagen
 - DTU Nutech at Risø, Denmark

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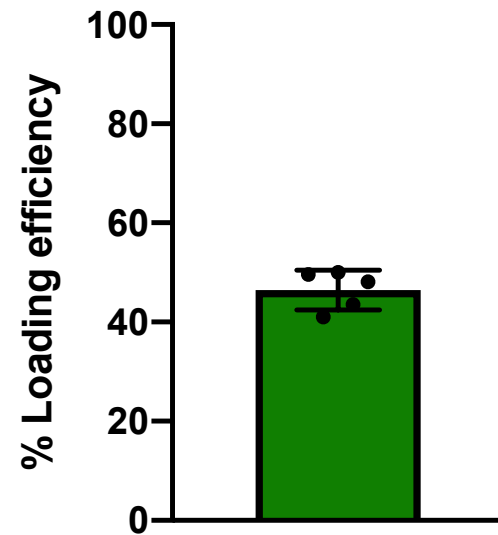


ново
nordisk
fonden



Bonus data

Radioactivity loading efficiency



Free micelles 24 h

