



IFIGENEIA

Innovative Facility for Isotope GENERation
with Efficient Ion Accelerator

WP4 – Radioisotope production and radiopharmaceuticals

T4.3 – T4.5 DKFZ's participation

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^{177}Lu -based targeted radiotheranostics – general design



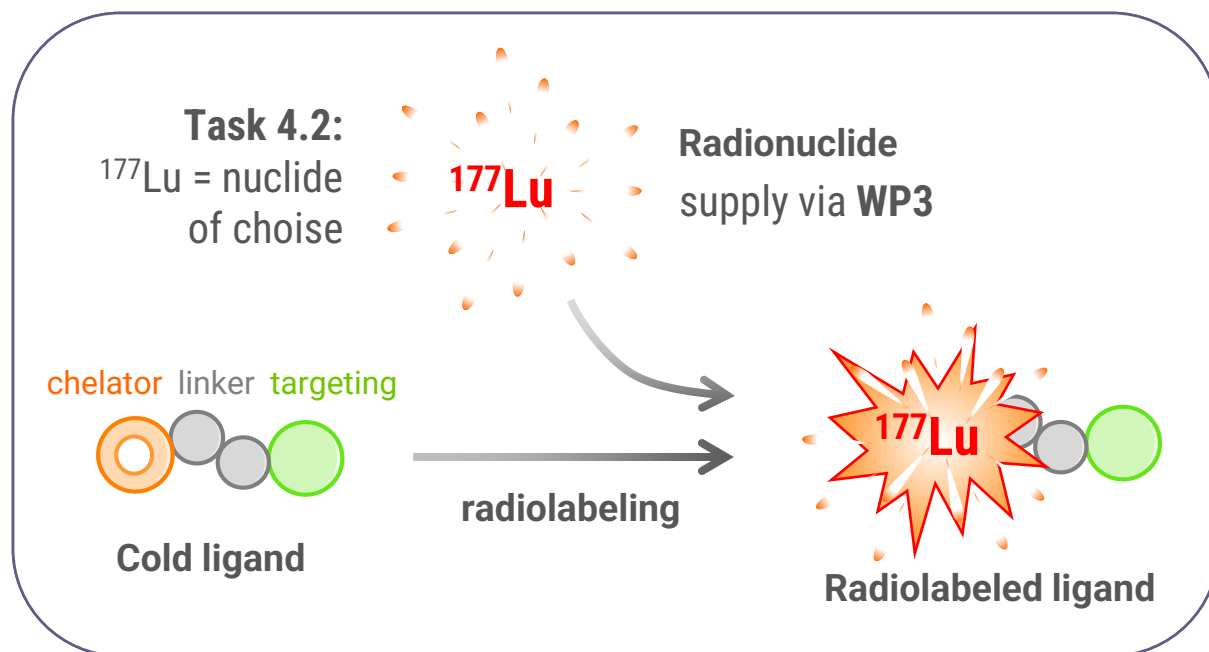
Task 4.2:
 ^{177}Lu = nuclide
of choice



**Radionuclide
supply via WP3**

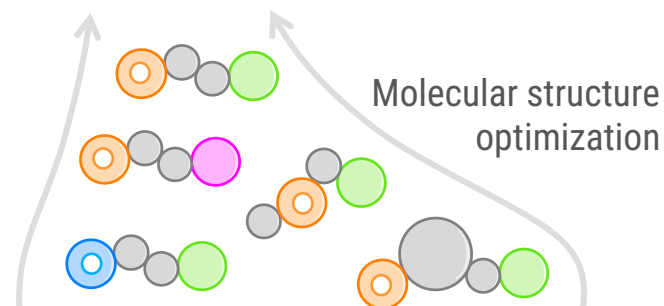
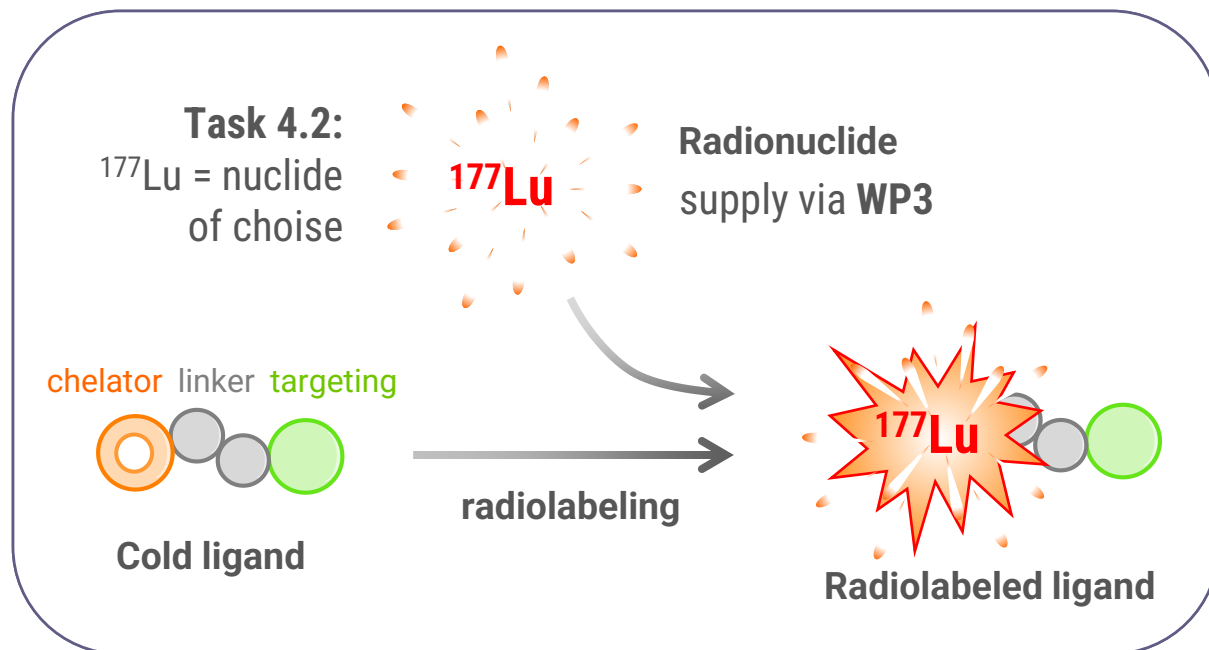


^{177}Lu -based targeted radiotheranostics – general design





Radiotheranostics – development workflow (T4.3 – T4.5)

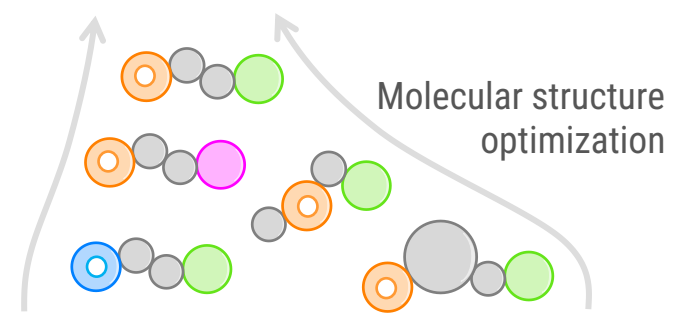
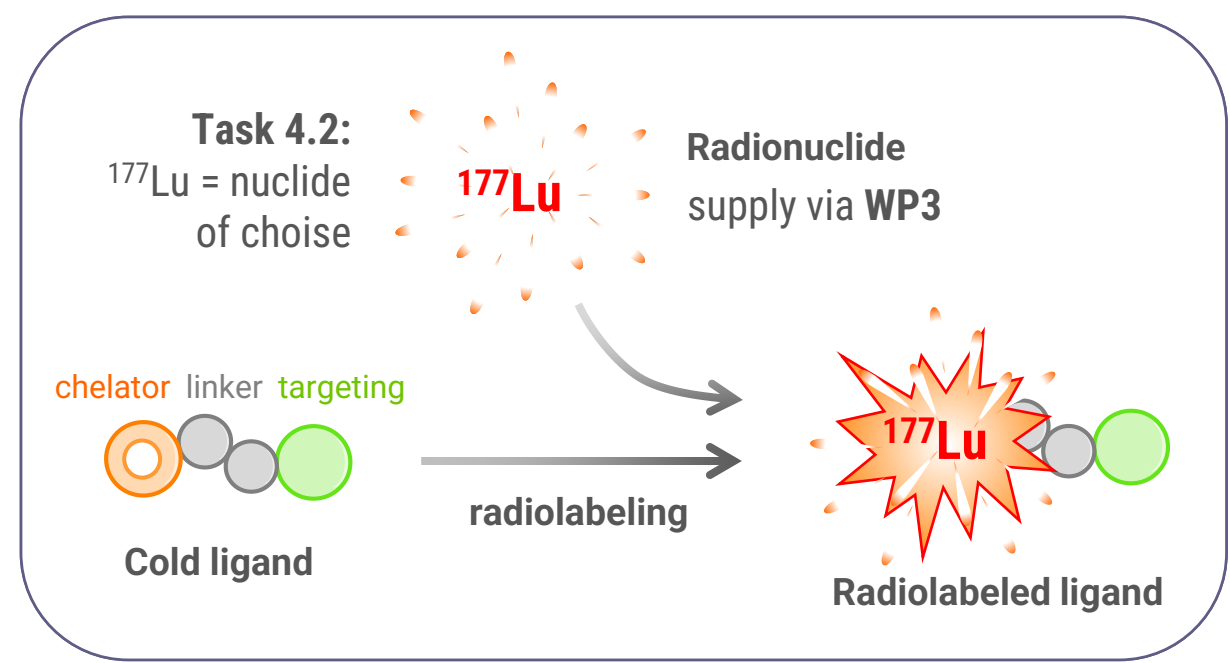


Task 4.3: Ligand development

Task 4.4:
Radioactively labeled ligand & quality control

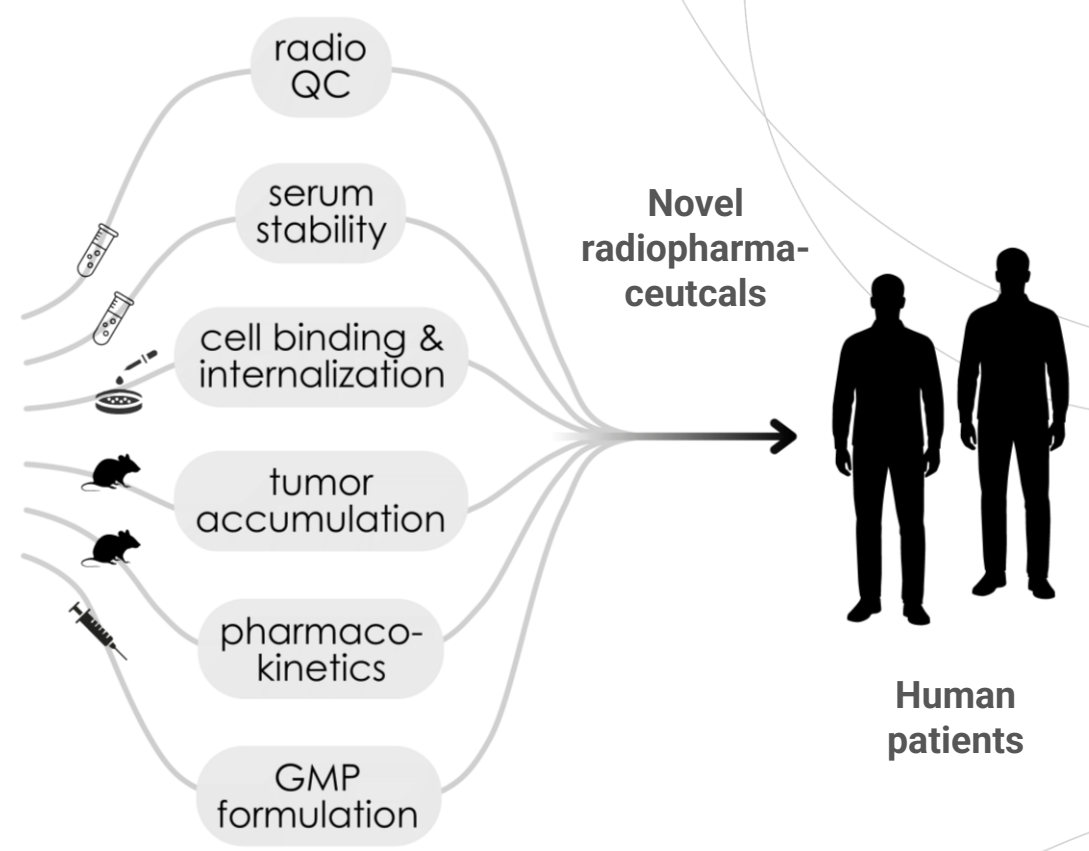


Radiotheranostics – development workflow (T4.3 – T4.5)



Task 4.3: Ligand development

Task 4.4:
Radioactively labeled ligand & quality control



Task 4.5:
Preclinical evaluation



Radiolabeling (T4.4)



Supply via **WP3**

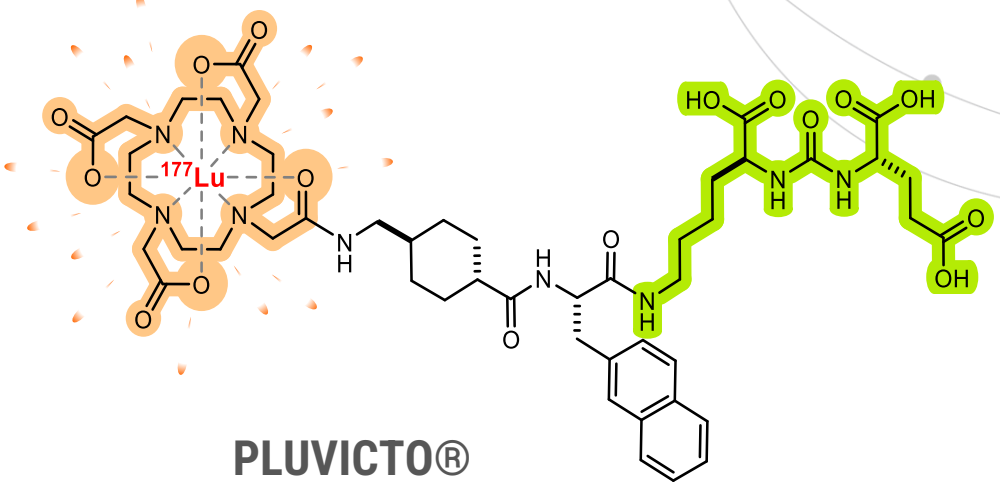
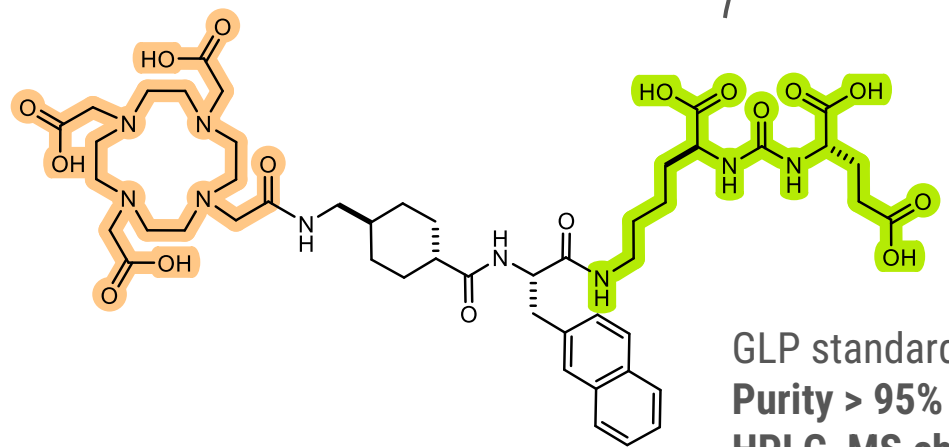
Radiolabeling optimization

Screening of conditions:
pH – buffer – temperature – molar activity

European Pharmacopoeia standards:
Sufficient molar activity
Ultrapure, metal free
Solvent: diluted HCl

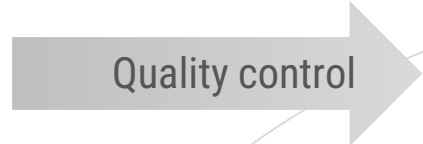
95°C
25 min

pH 4.5
NaOAc



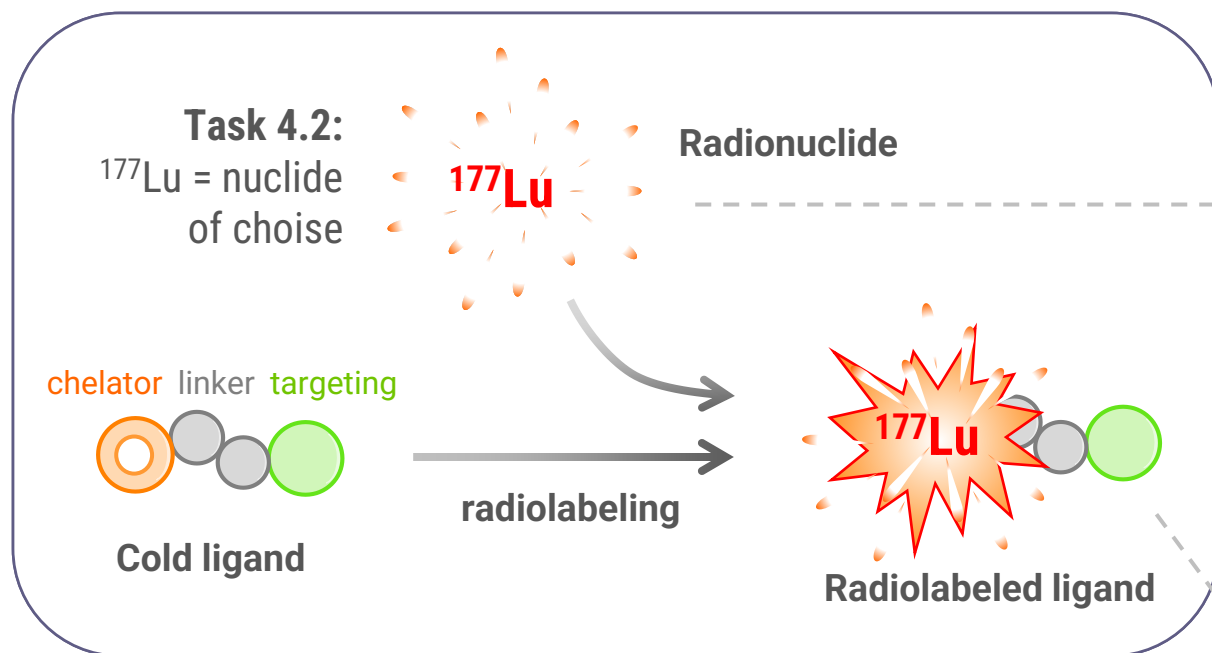
PLUVICTO®
GLP standard
(research purpose)

GLP standards:
Purity > 95%
HPLC, MS characterization
Solvent: ultrapure water

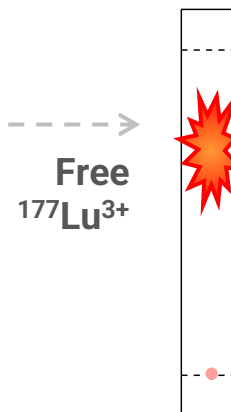




Radiotheranostics – quality control (T4.4)



RadioTLC



RadioHPLC



OR

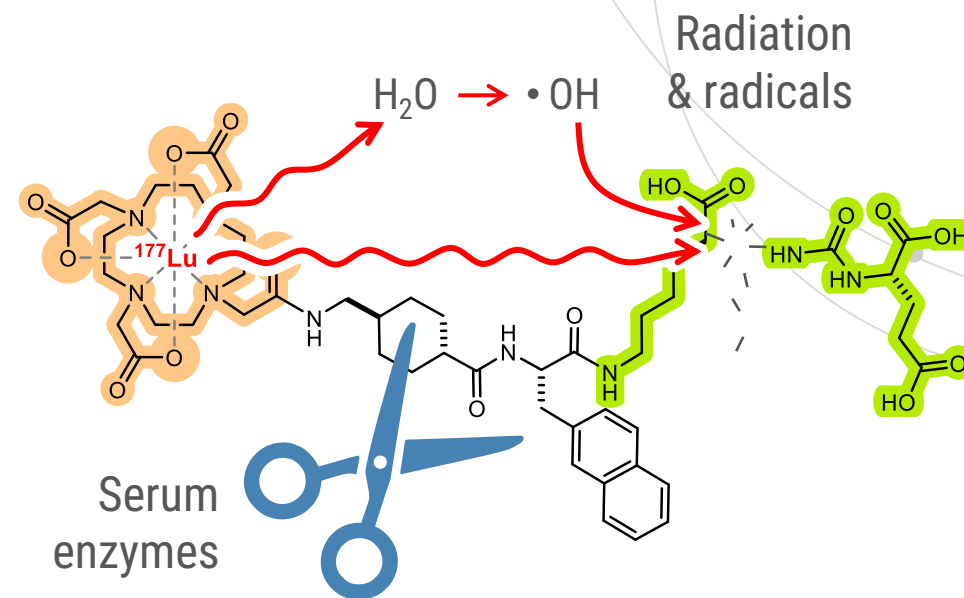
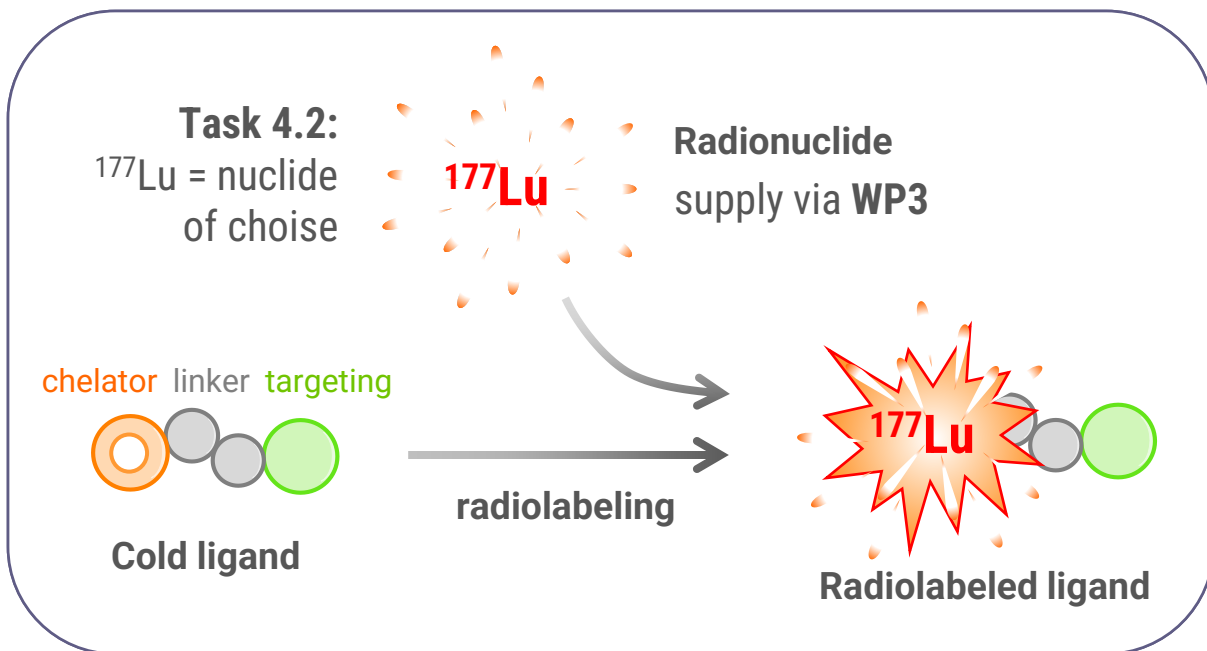


Chromatographic methods:
Reverse-phase radioHPLC
& radioTLC (thin-layer chromatography)

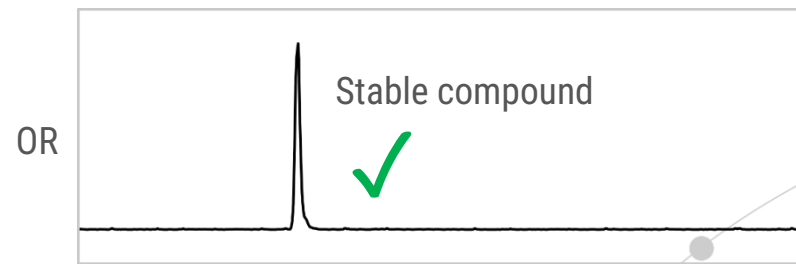
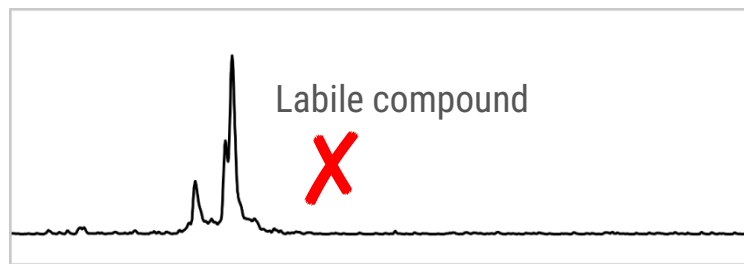
Radiolabeled ligand



Radiotheranostics – stability (T4.4)



Chromatographic methods:
RP-radioHPLC



Radiotheranostics – *in vitro* (T4.4)

Task 4.2:
 ^{177}Lu = nuclide
of choice



chelator linker targeting

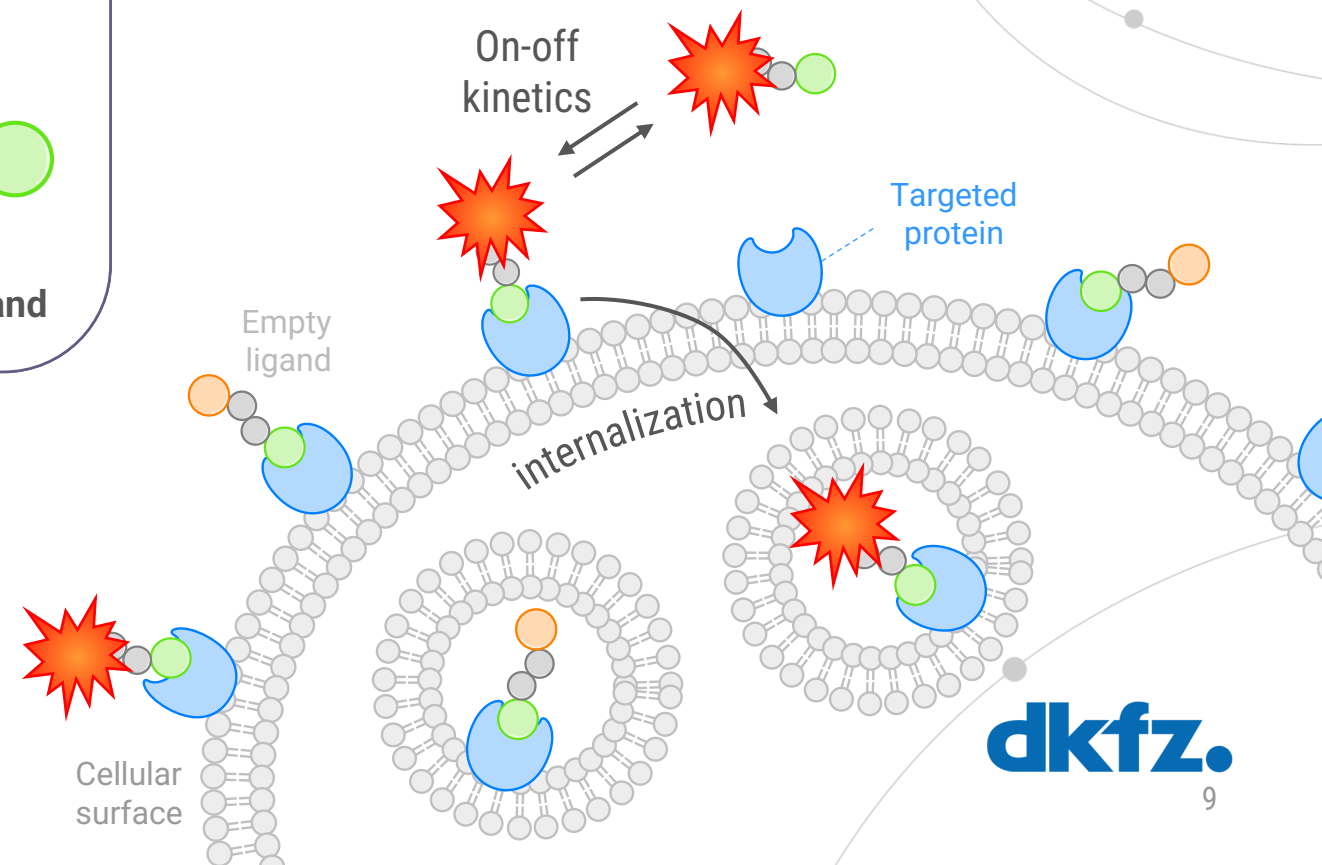
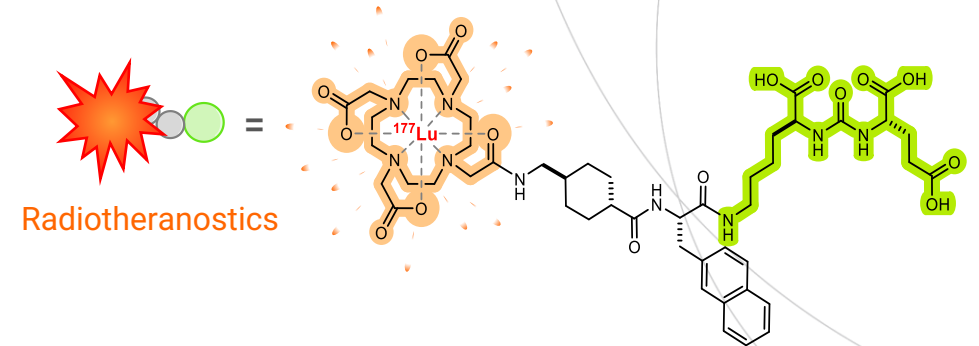


radiolabeling

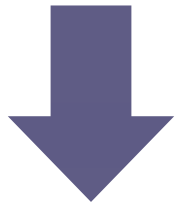


Cellular assays:

- ✓ Binding affinity
- ✓ Total cellular binding
- ✓ Internalization



- ✓ Radiolabeling & quality control (T4.4)
- ✓ (Radio)chemical & Serum stability (T4.4)
- ✓ *In vitro* evaluation (T4.4)

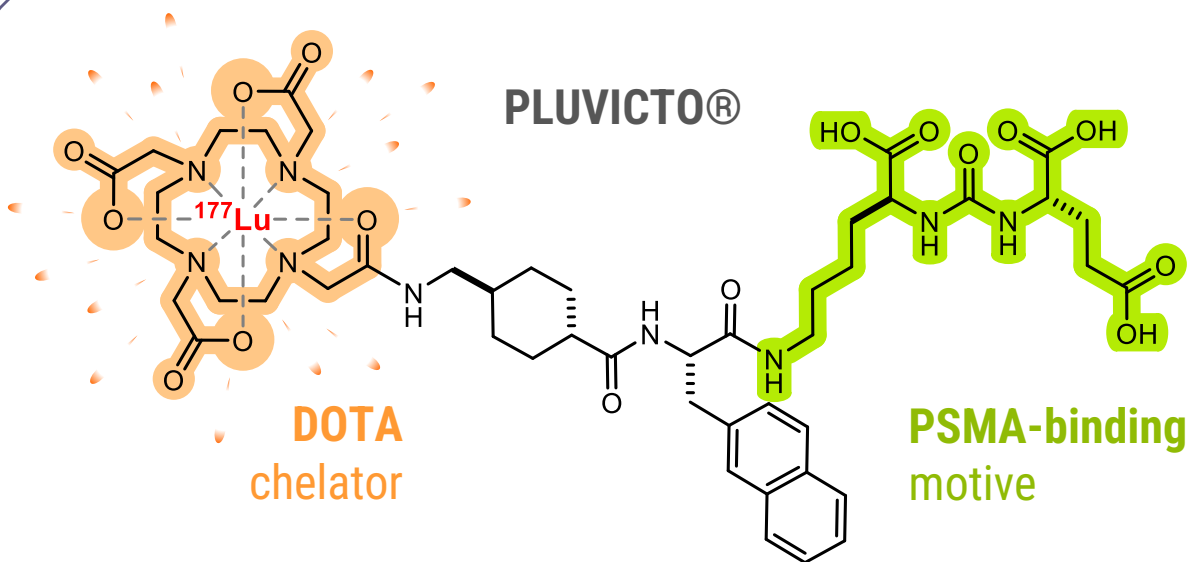


Development of novel radiopharmaceuticals (T4.3)





New generation of PSMA-targeted radiopharmaceuticals (T4.3)



Indication: Metastatic Castration-Resistant Prostate Cancer
Targeting: Prostate-Specific Membrane Antigen (**PSMA**)

Limitations:

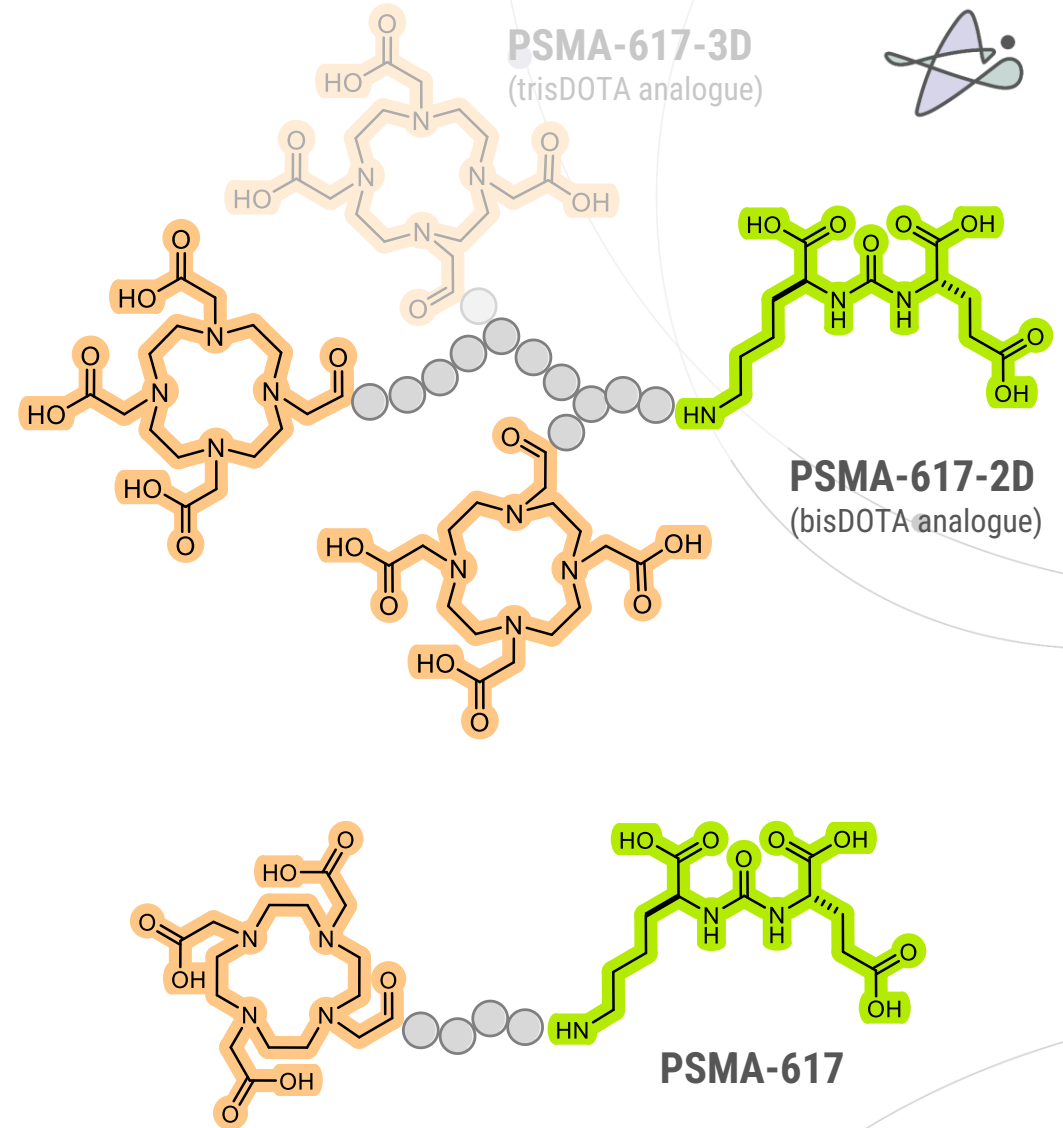
- ~ 50% patients without response
- Resistance development

New generation of PSMA-targeted theranostics

New generation of PSMA-targeted radiopharmaceuticals (T4.3)

Strategy:

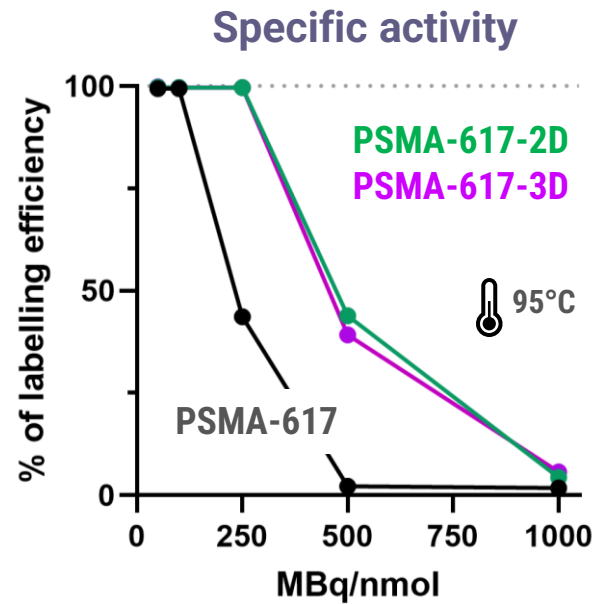
Multiple chelation sites → elevated molar activity
→ → higher radiation dose



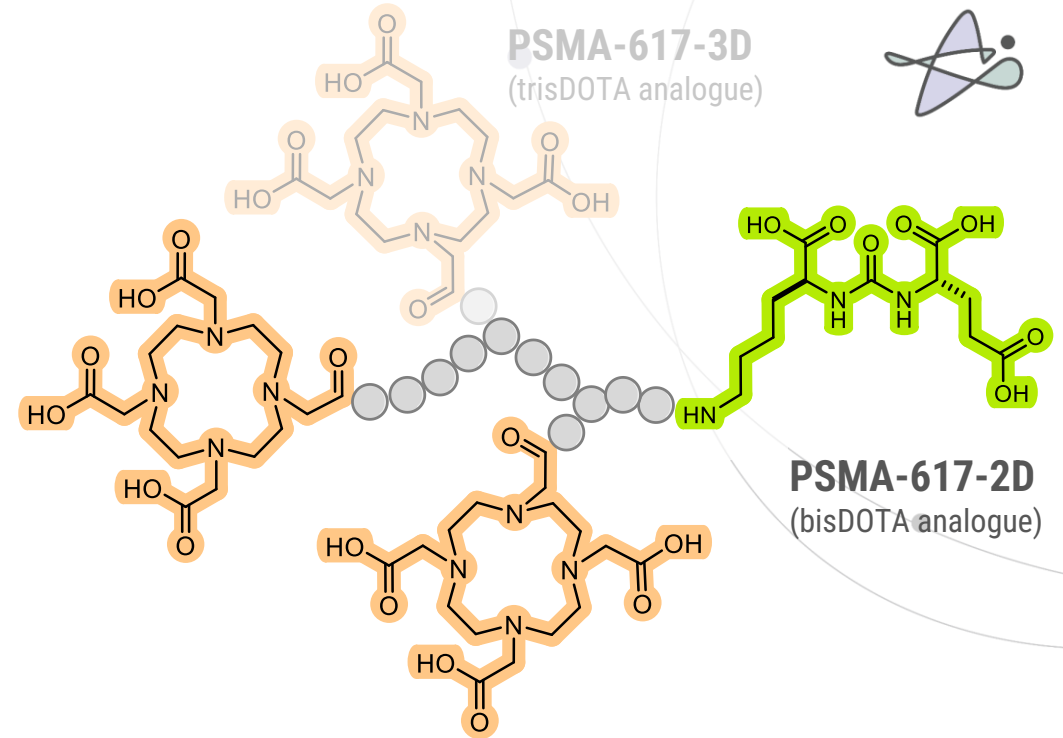
New generation of PSMA-targeted radiopharmaceuticals (T4.3 & T4.4)

Strategy:

Multiple chelation sites → elevated molar activity
→ → higher radiation dose



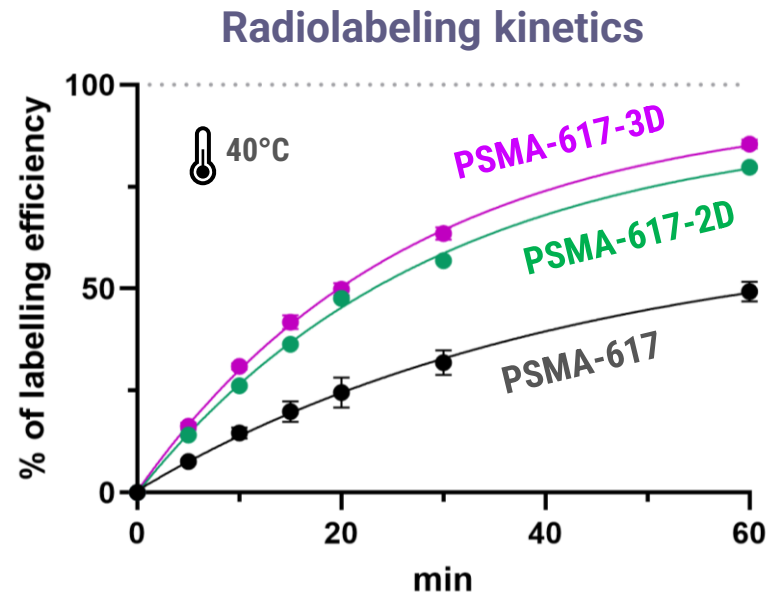
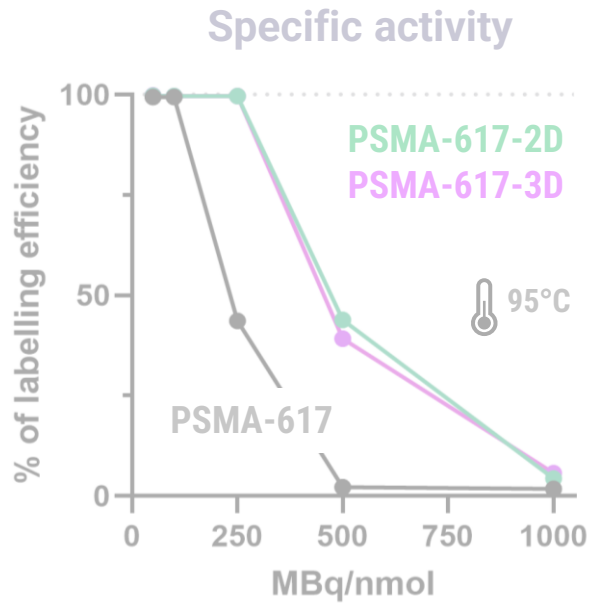
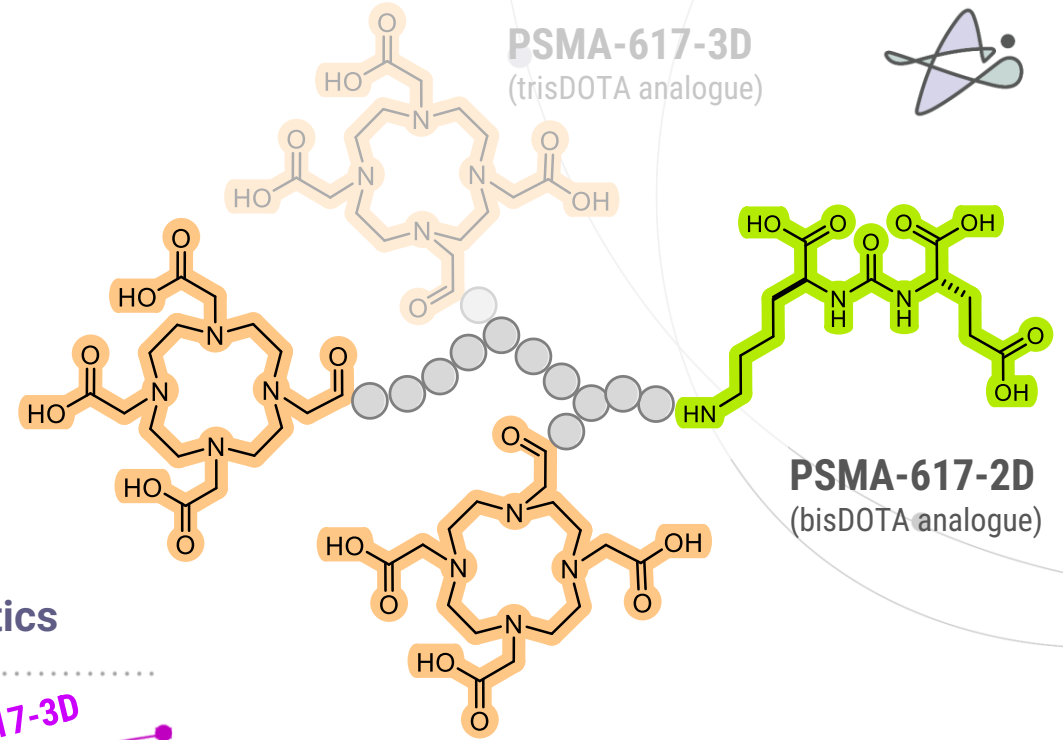
PSMA-617-2D/3D reached elevated **molar activity**



New generation of PSMA-targeted radiopharmaceuticals (T4.3 & T4.4)

Strategy:

Multiple chelation sites → elevated molar activity
 → → higher radiation dose

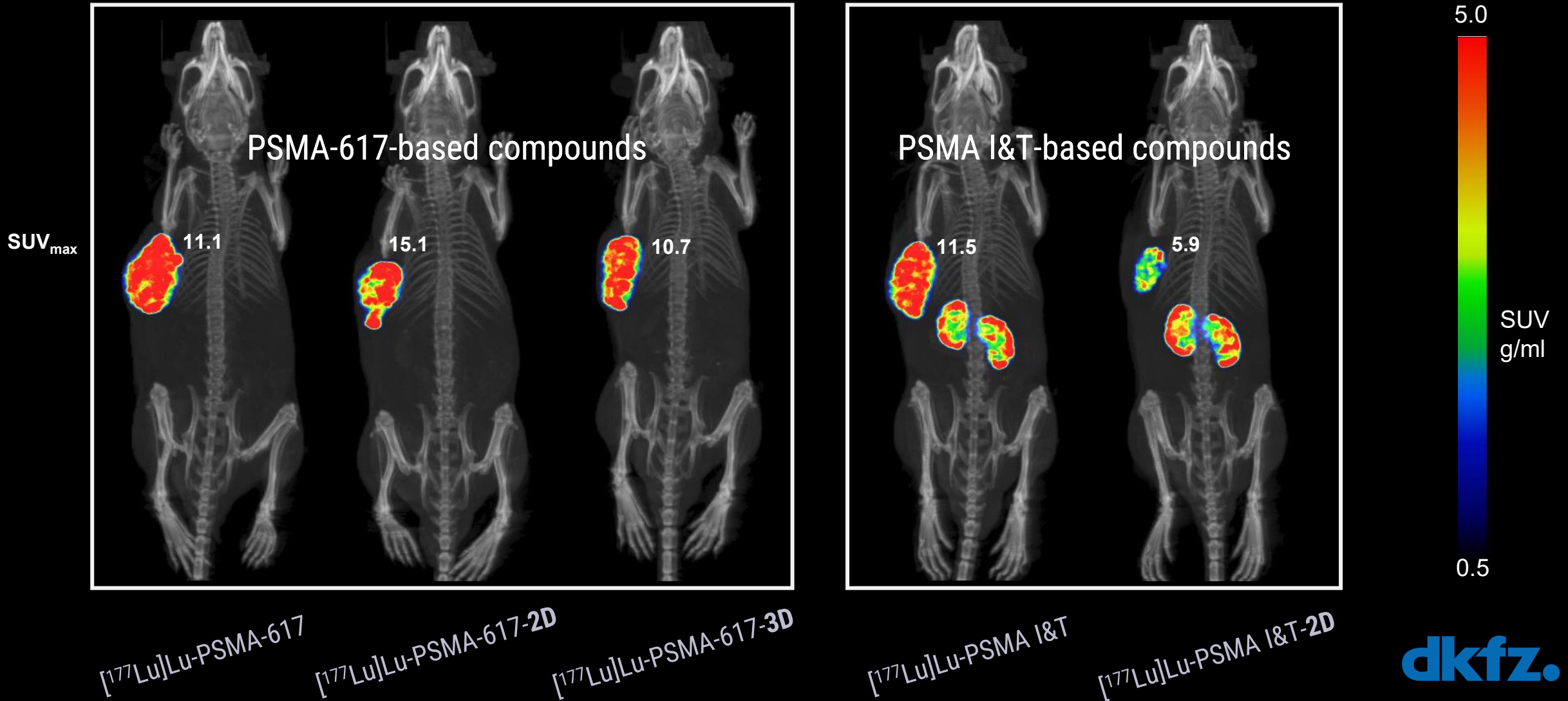


PSMA-617-2D/3D reached elevated labeling rate

New PSMA-targeted radiopharmaceuticals

Preclinical evaluation (T4.5)

SPECT/CT – 24 h p.i.





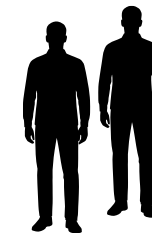
Research purpose vs clinical application (T4.5)

Research purpose



- **In-house supply**
- **GLP standards** (Good laboratory practice)
= standard laboratory procedure
- Manual / automated synthesis
- Manual radiolabeling
- Sterile GLP formulation for *in vivo*
- Safety precautions
- Chemical purity > 95%
- Radiochemical purity > 95%

Clinical applications



- **Official suppliers** of radiopharmaceuticals
- **GMP standards** (Good manufacturing practice)
= additional development of GMP procedure
- (Semi)Automated synthesis
- (Semi)Automated radiolabeling and purification
- Sterile GMP formulation
- Certified clean laboratories
- Extensive administration
- European Pharmacopoeia standards

Next steps

> T4.3

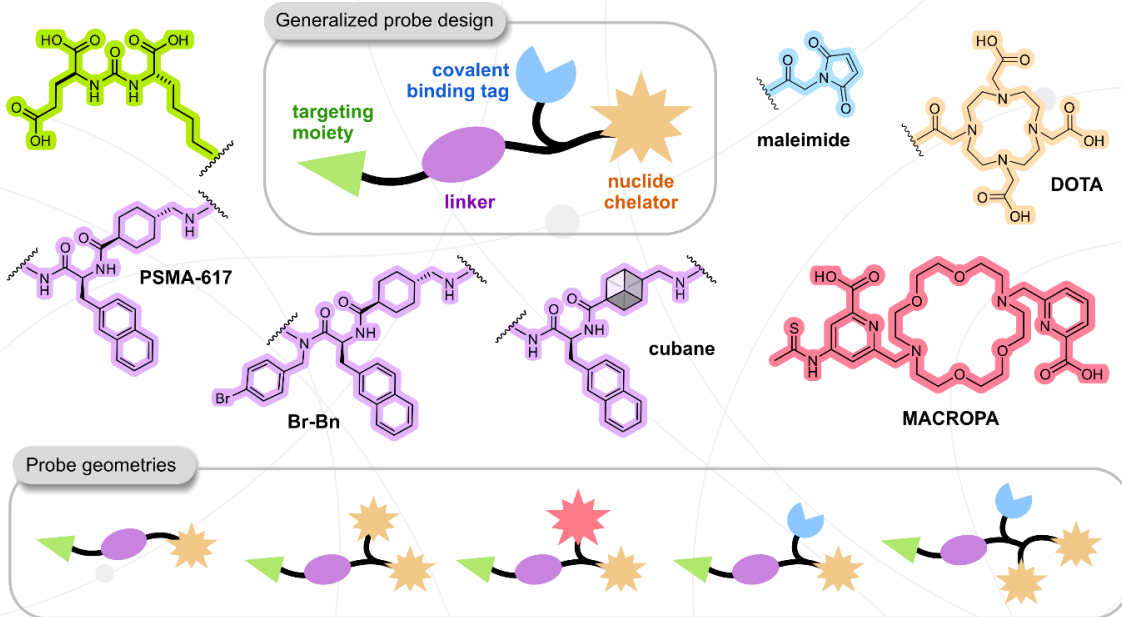
- > Follow-up study on PSMA-targeted ligands

> T4.4

- > Optimization of radiolabeling conditions for ligands chosen in T4.3
- > Preparation of protocols and training

> T4.5

- > Preclinical evaluation of chosen ligands from T4.3 and T4.4
- > Preparation of protocols



Joao
Seco



Martina
Benešová-Schäfer



Thank you for your attention



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