

Innovative Methoden der experimentellen und klinischen Bildgebung zur Detektion von invasiven Aspergillosen

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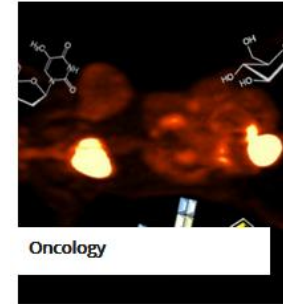


Werner Siemens Imaging Center:

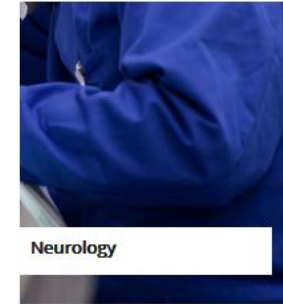


**Universitätsklinikum
Tübingen**

**Prof. Dr. Pichler
Chair & Director**



Oncology



Neurology



Immunology/Inflammation



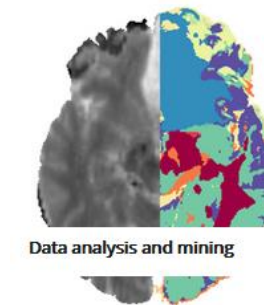
Imaging Science



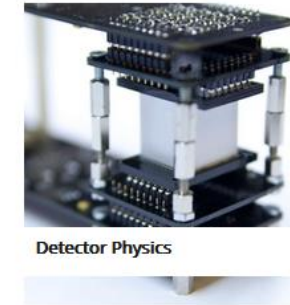
Imaging Probe
Development



Translational Research

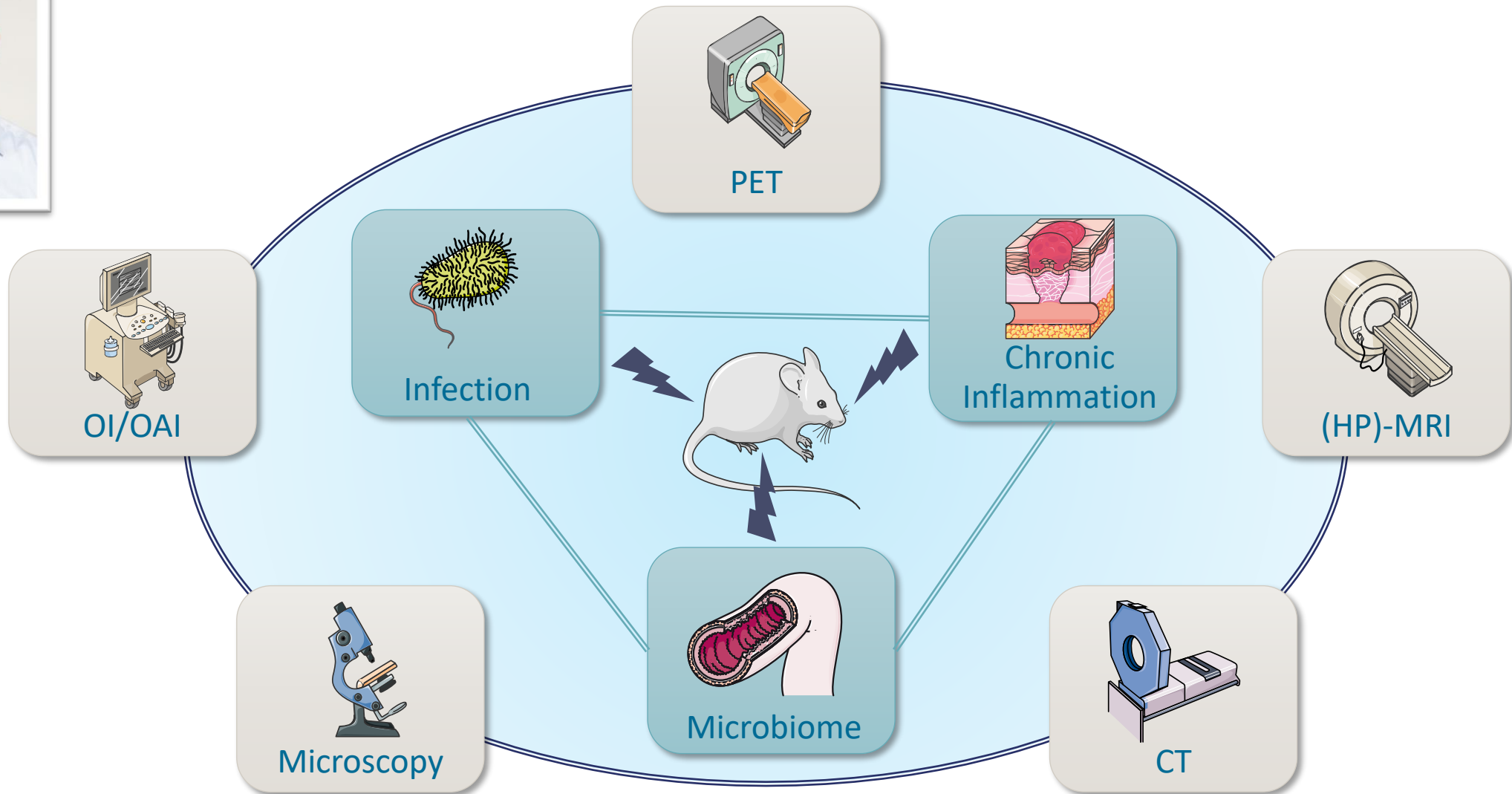
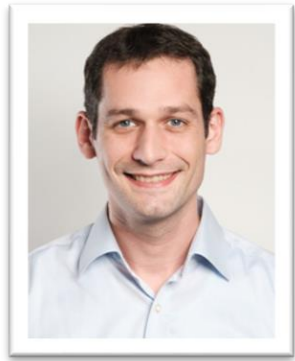


Data analysis and mining

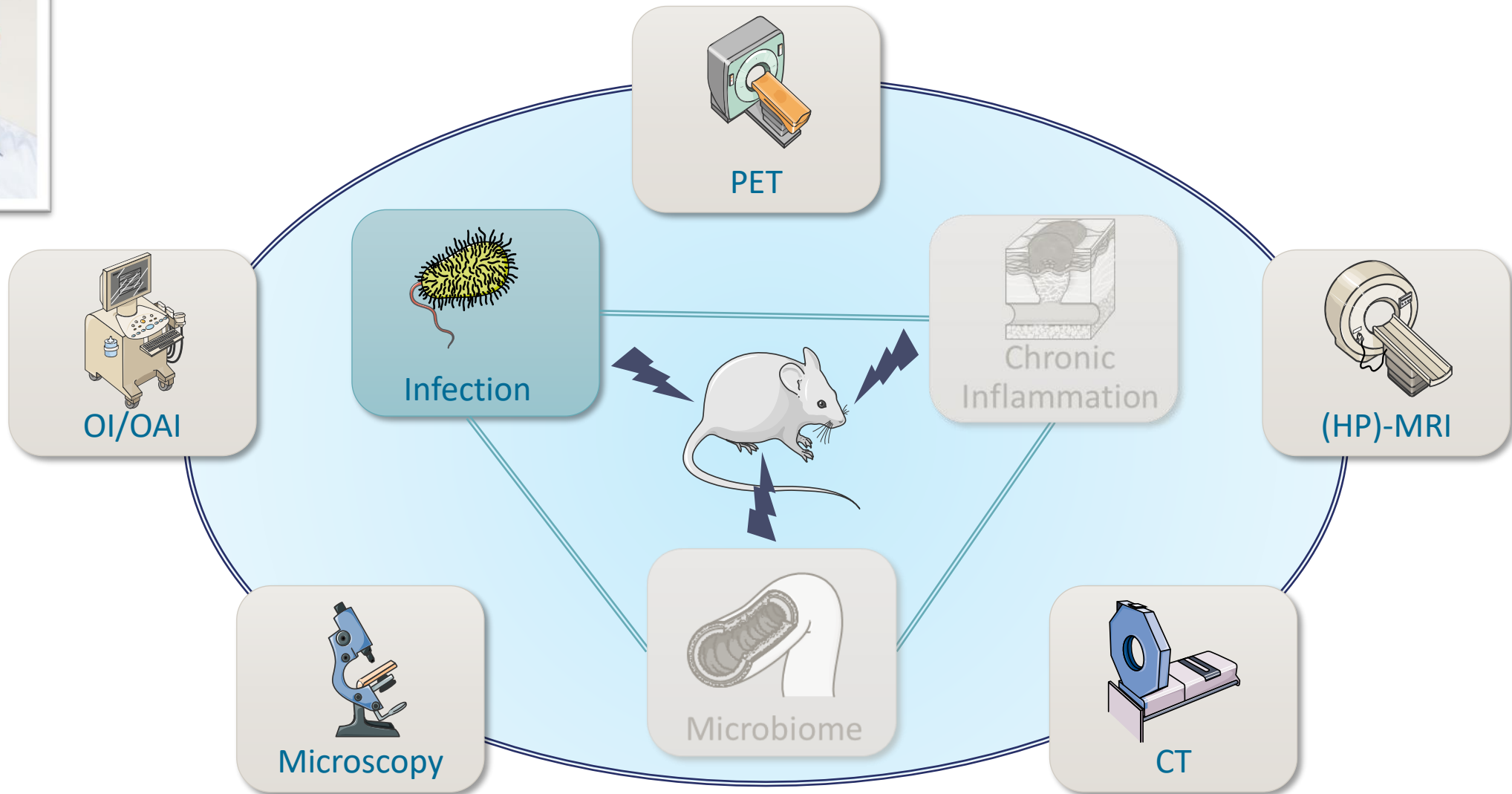


Detector Physics

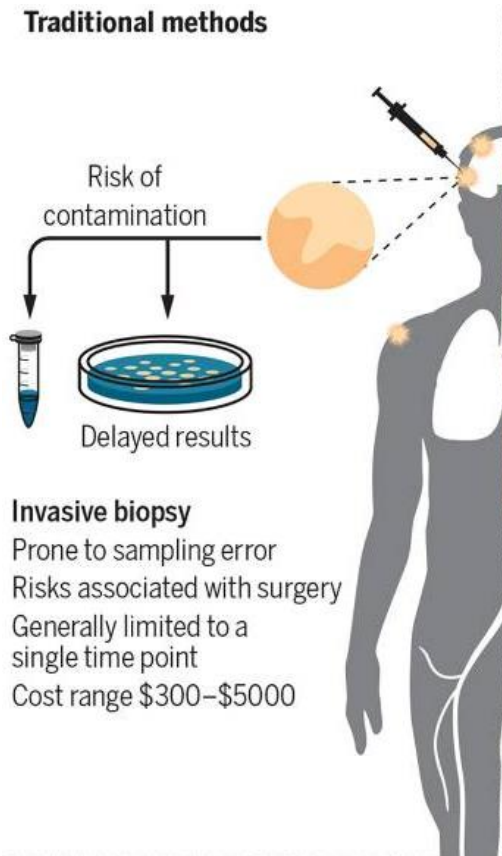
Inflammation and Infection Imaging



Inflammation and Infection Imaging



Diagnostic of infections



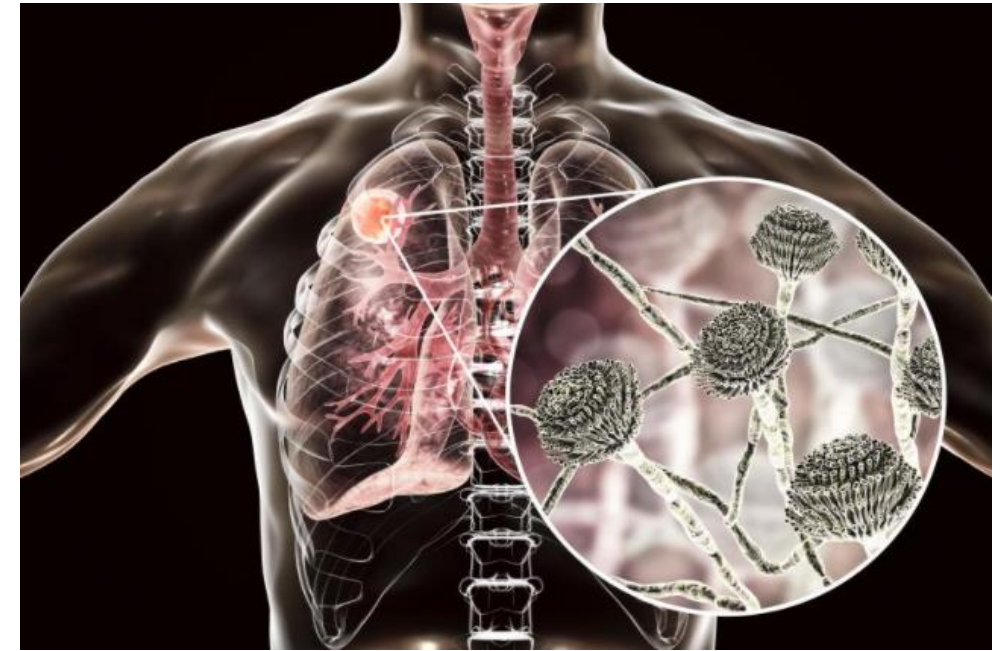
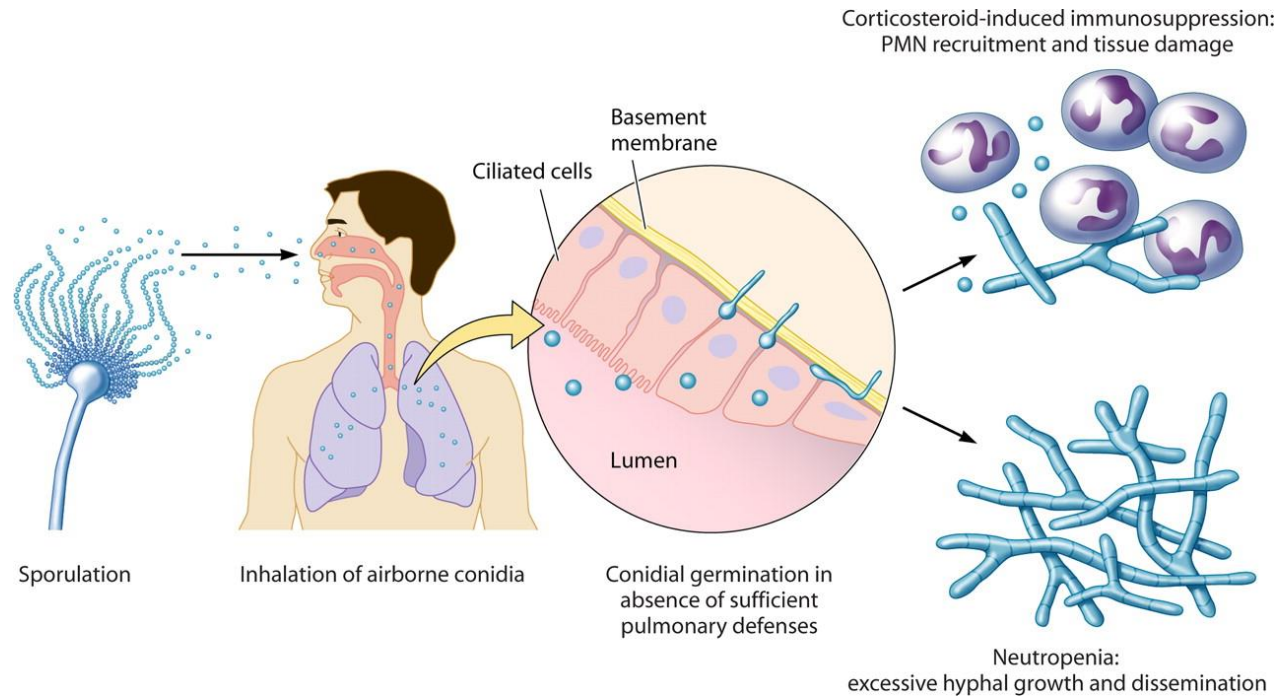
Ordonez et al. Sci. Transl. Med. 2019

2022

- ^{18}F -FDG (glucose metabolism)
- Radiolabeled leukocytes
- Radiolabeled antibiotics
- 2- ^{18}F -fluorodeoxyribose
- 2- ^{18}F -PABA
- ...

**Specific tools needed
to unlock personalized medicine**

Aspergillosis: a deep seated fungal infections



**Gap between suspicion – diagnosis – therapy
+ resistant spores**

Routine aspergillosis diagnosis

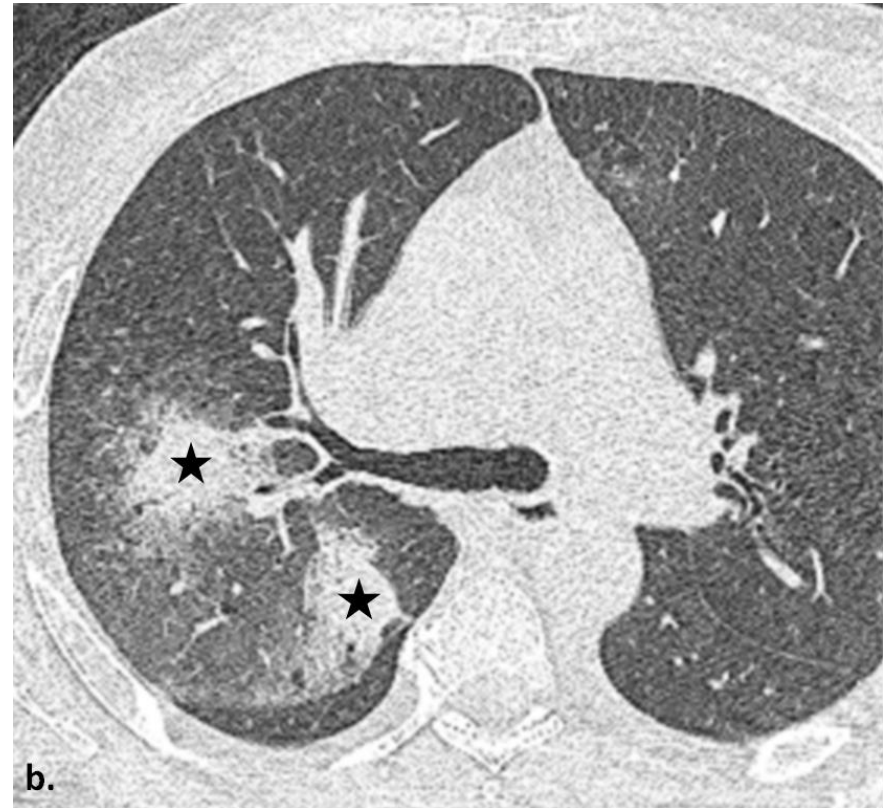
1. Clinical observation

- > Fever of unknown origin (antibiotic resistant)
- > Immunodepressed
- > Comorbidities (asthma, COPD)

2. Laboratory work

- > Broncho alveolar lavage
- > Biopsies
- > Blood tests

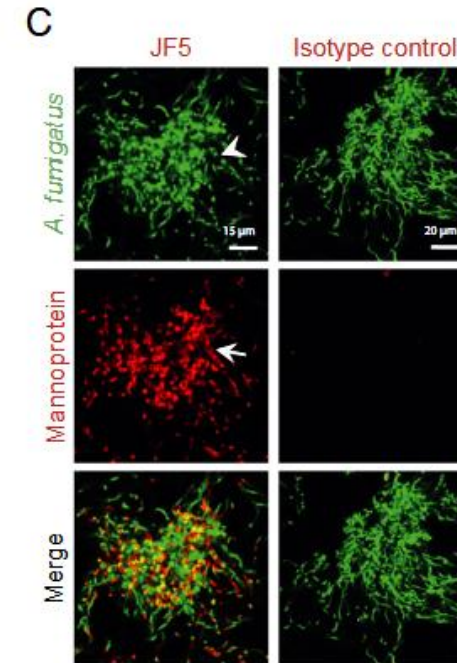
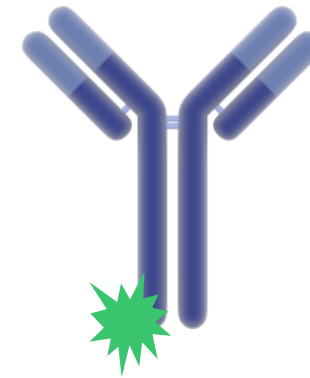
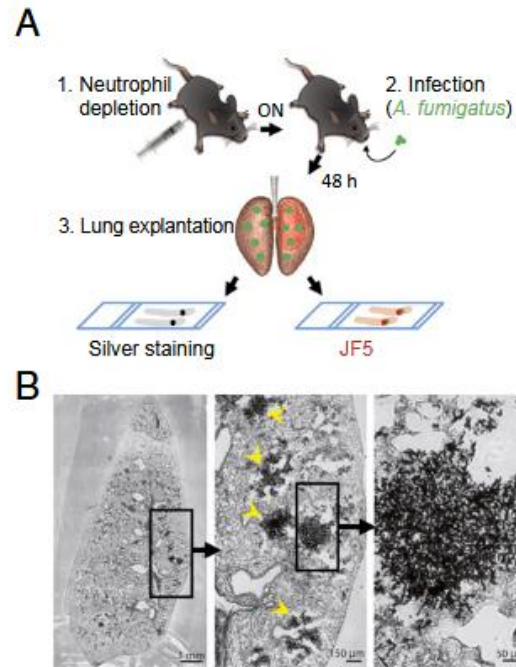
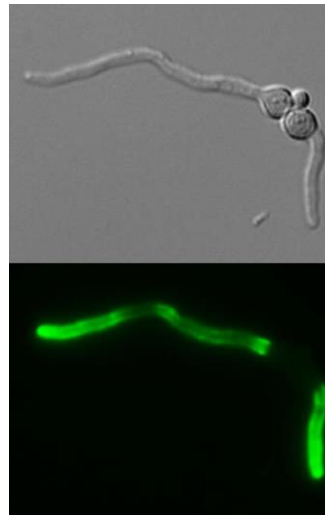
3. Imaging



JF5 antibody

Development of an anti-Galf mAb (JF5)

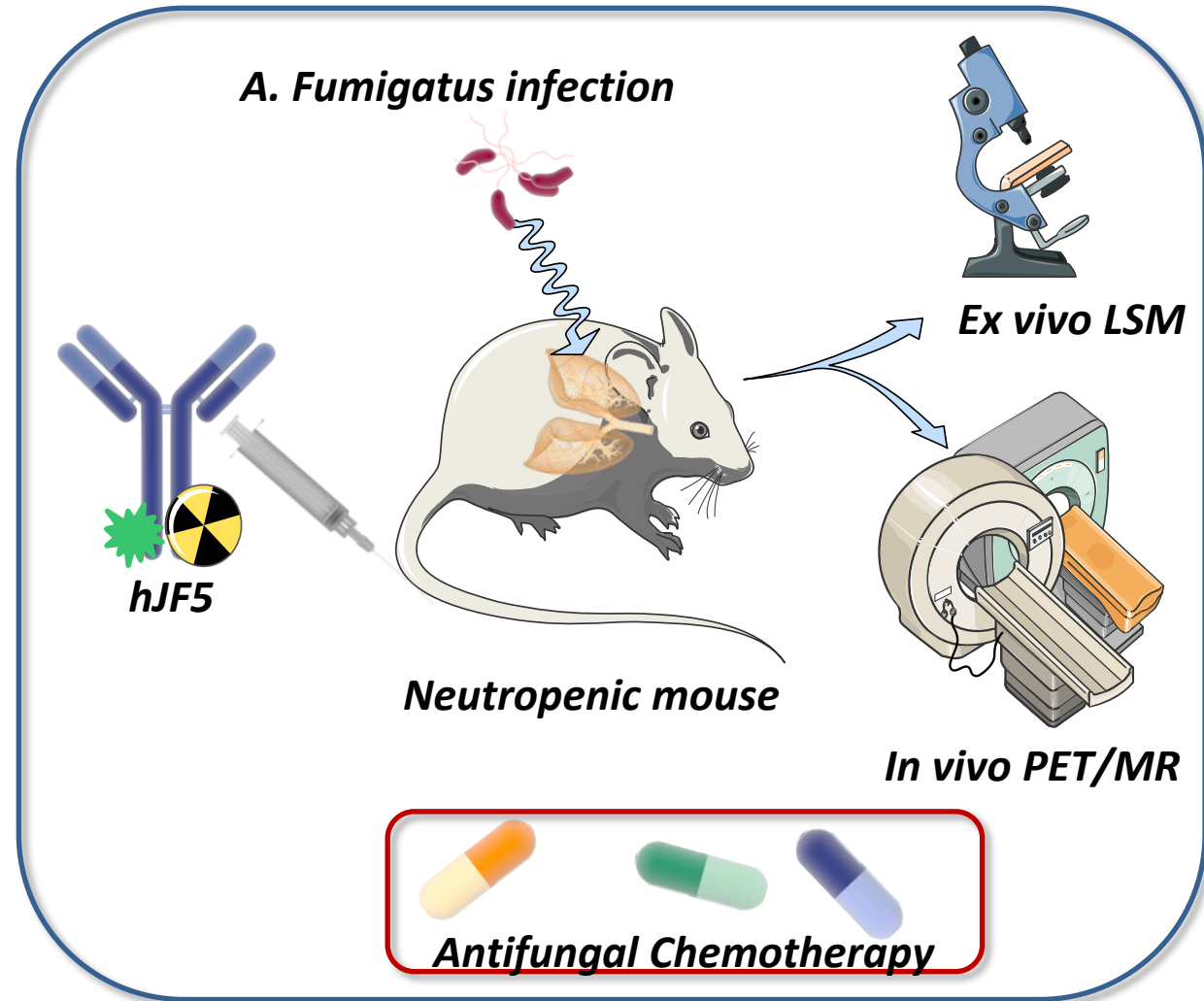
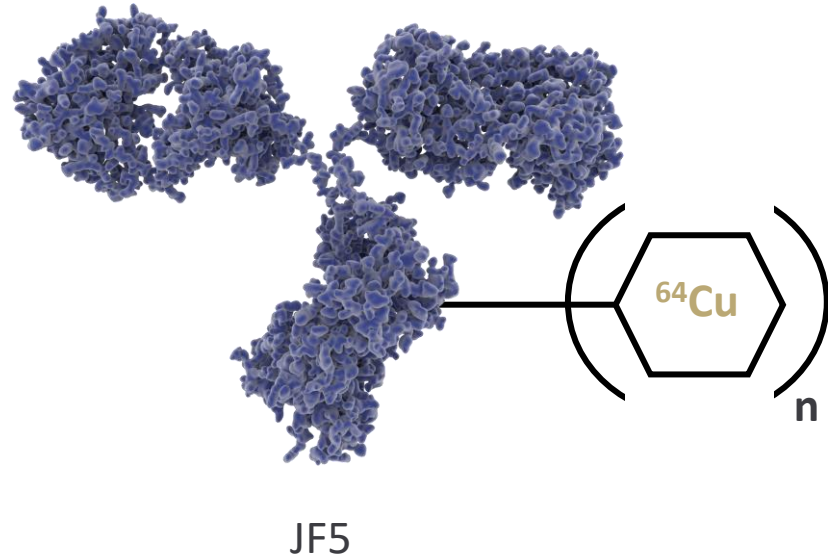
- Galf specific to *A. fumigatus* hyphae
- Detection *in vitro*, *ex vivo* and *in vivo*



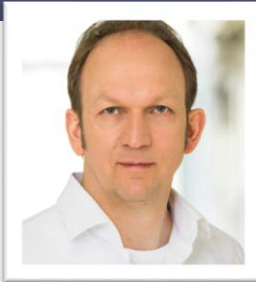
Prof. Thornton
(University of Exeter, UK)

Thornton, Clin. Vaccine Immunol. 2008, Rolle et al. PNAS 2016

Aspergillosis animal model

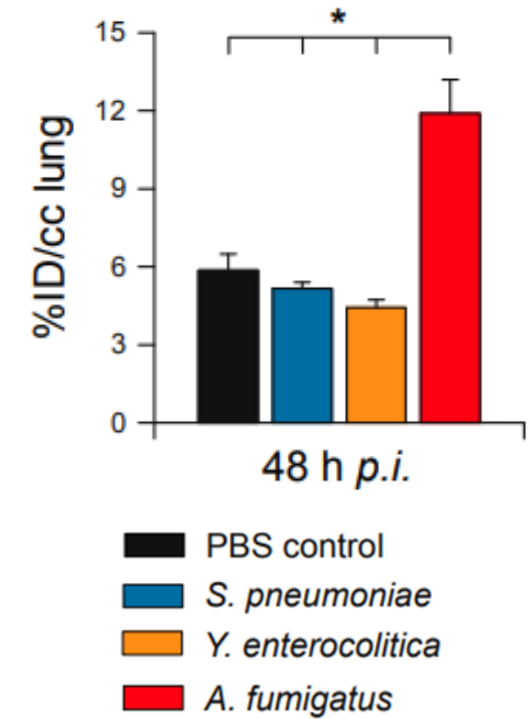
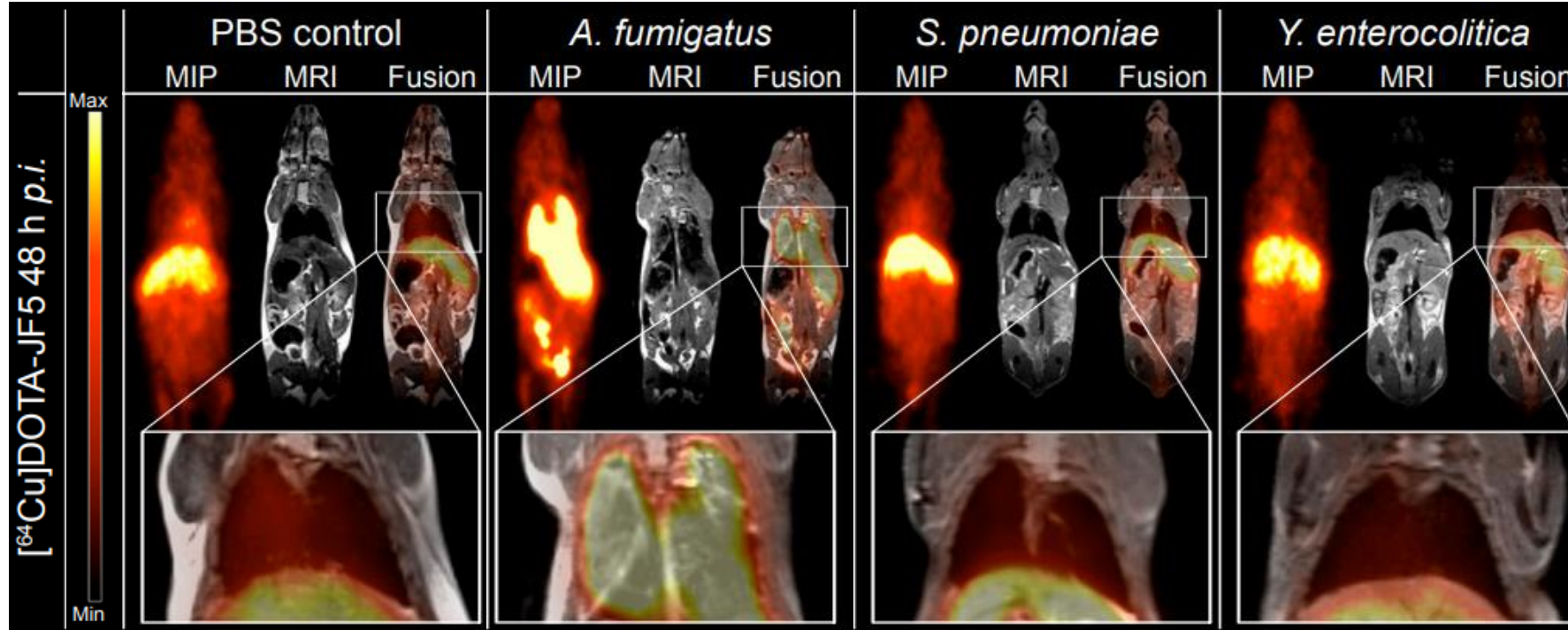


Preclinical IPA model



Prof. Gunzer
(UDE)

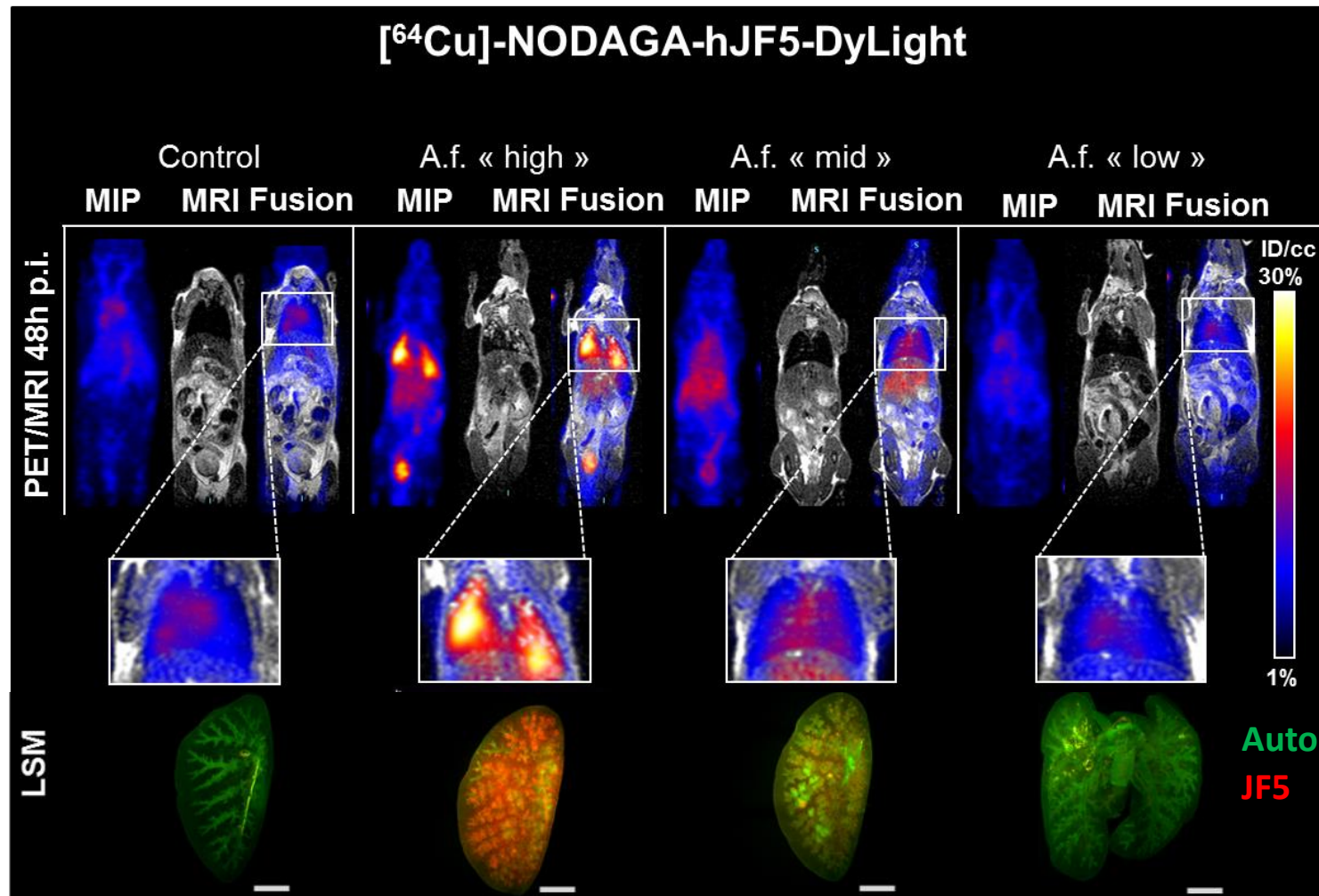
Specificity towards *A. fumigatus*



Rolle et al. PNAS 2016

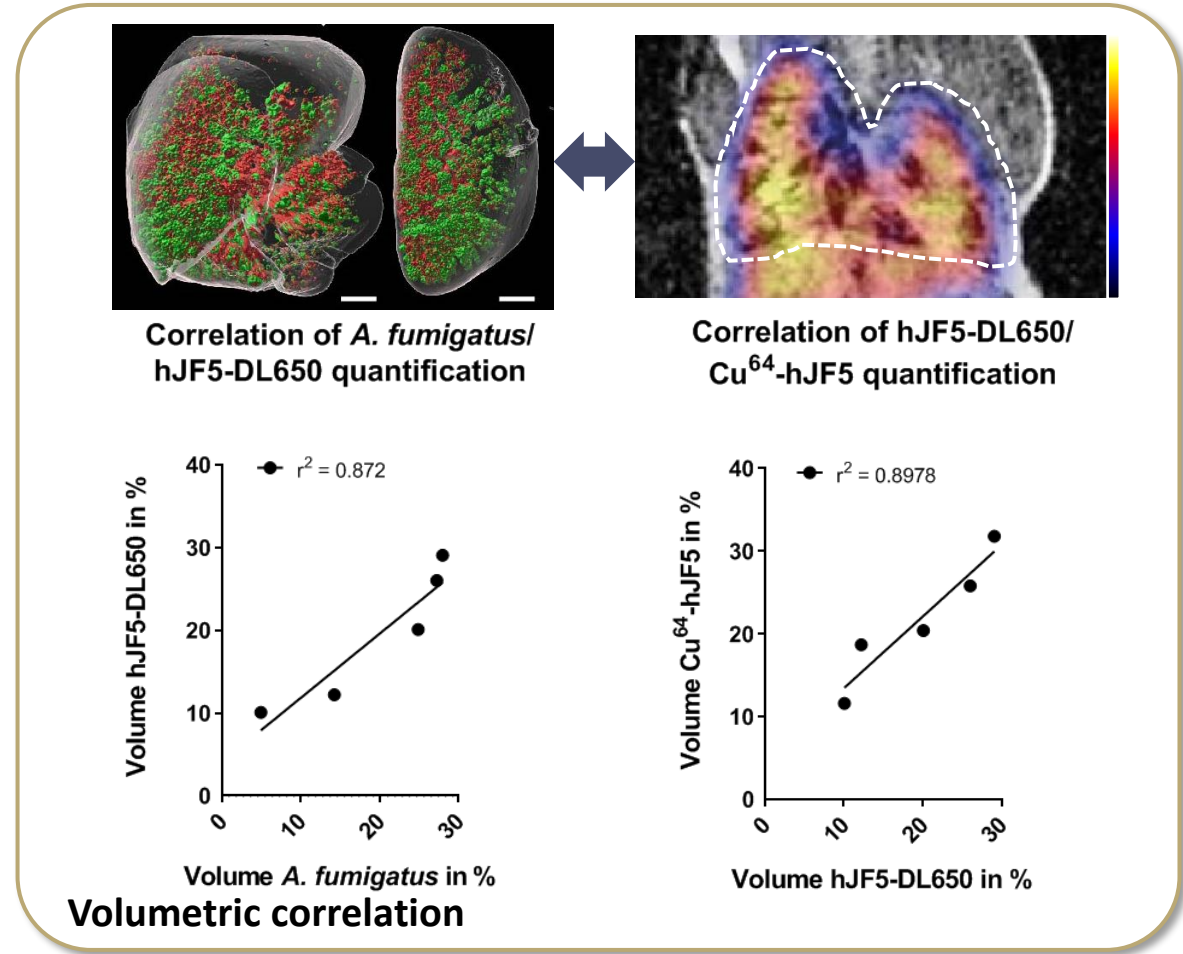
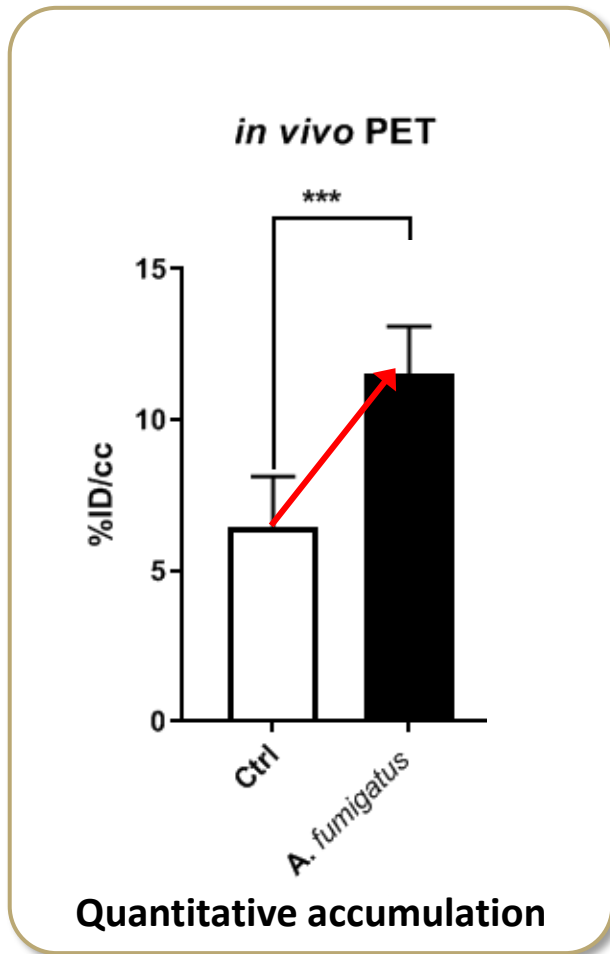
[⁶⁴Cu]NODAGA-hJF5:
highly specific, high contrast

Infection severity *in vivo* and correlation



Qualitative Correlation:
Infection and Radiotracer accumulation

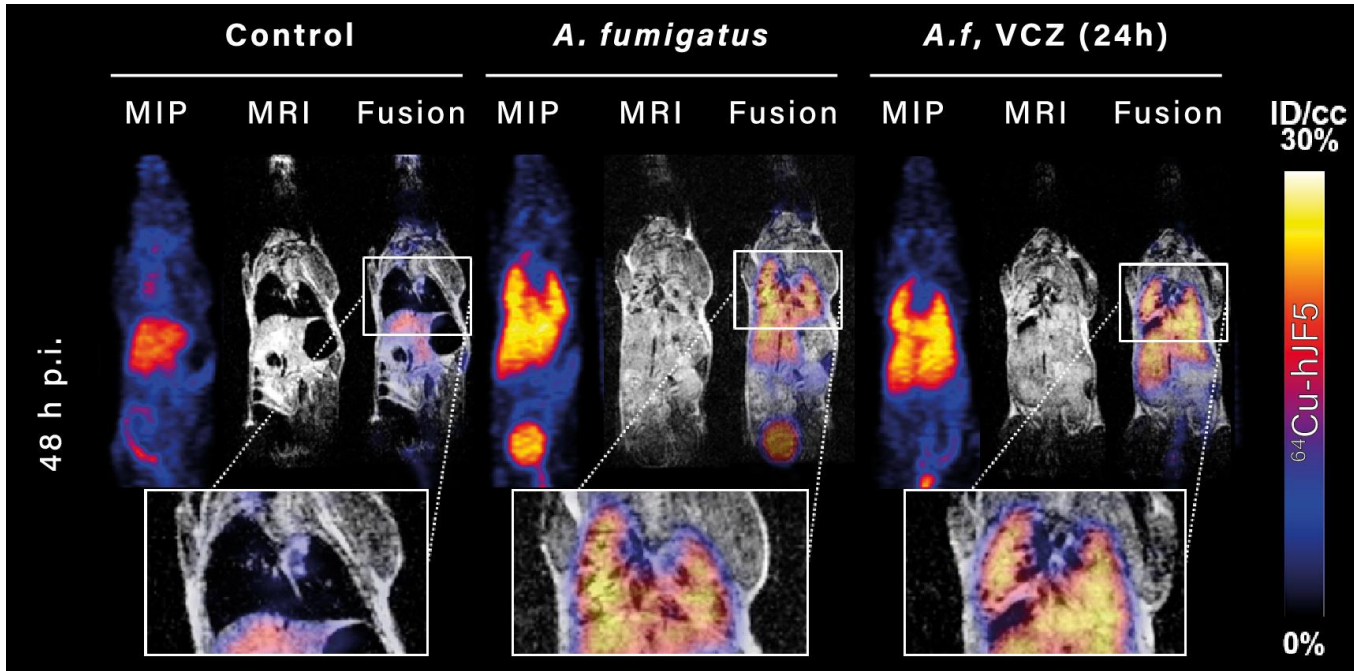
Infection severity *in vivo* and quantification



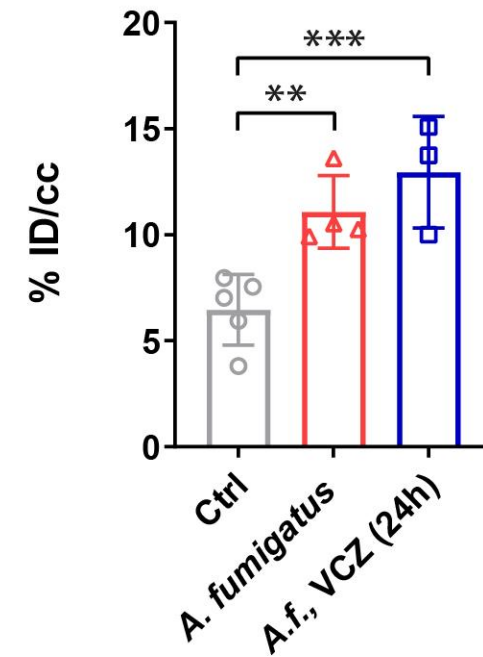
Henneberg et al. Nat Commun 2021

Quantitative Correlation:
Infection – Radiotracer occupancy

Therapy monitoring: late interventions

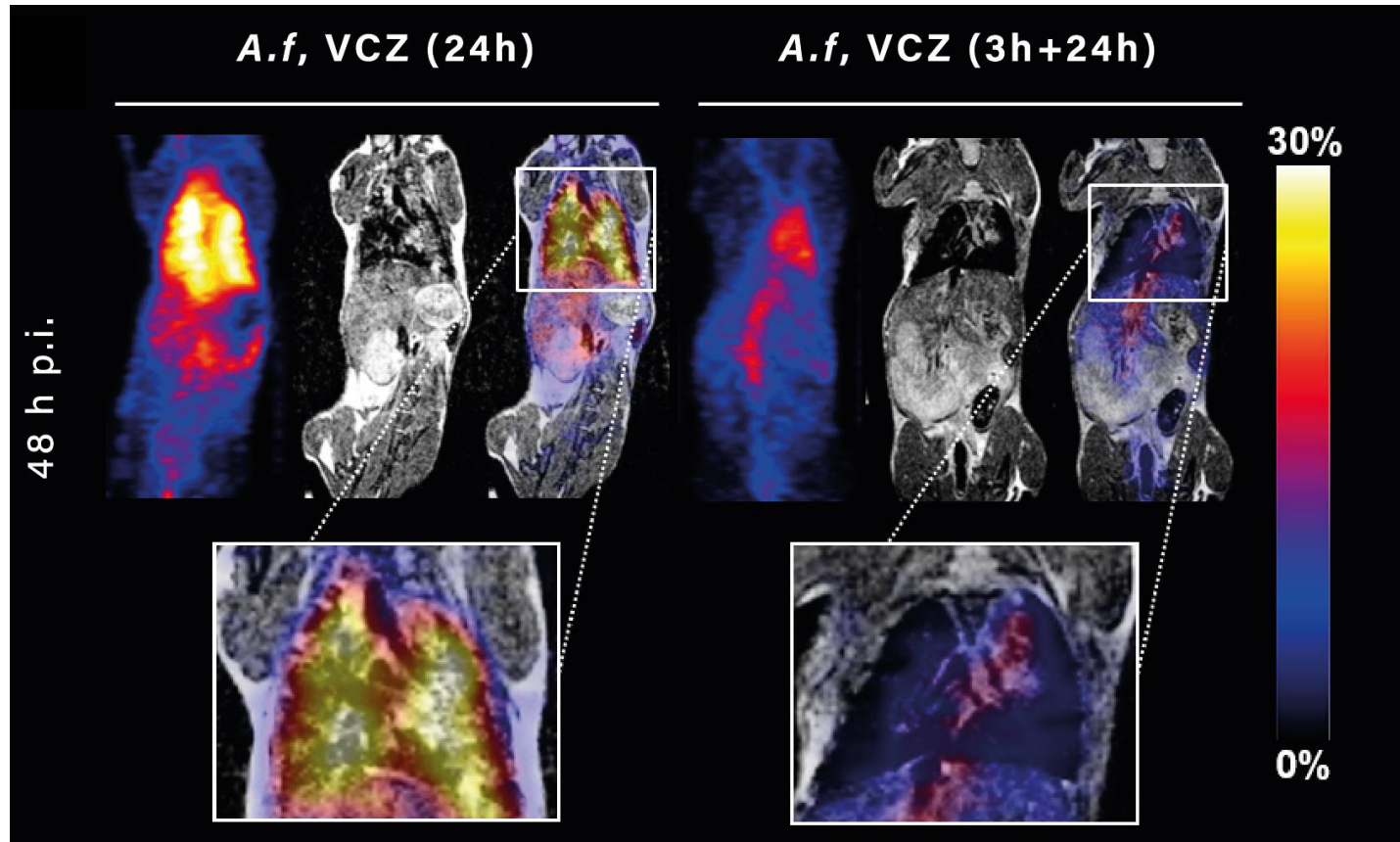


48 h p.i. *in vivo* PET



Henneberg et al. Nat Commun 2021

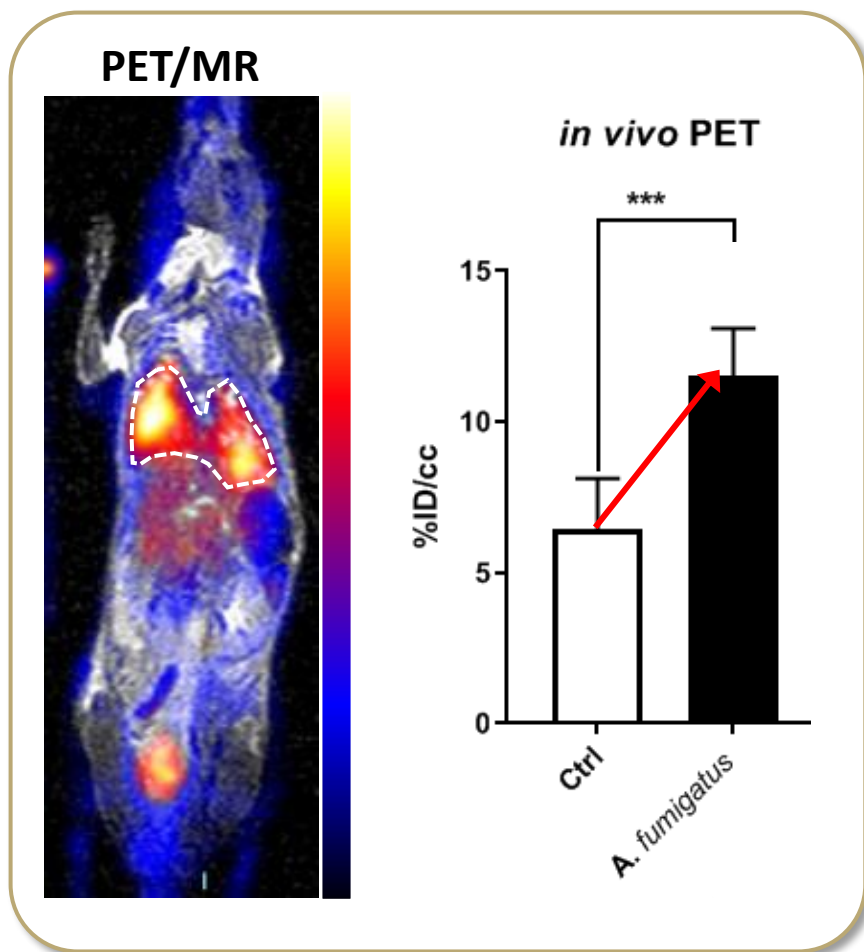
Intervention time points comparison



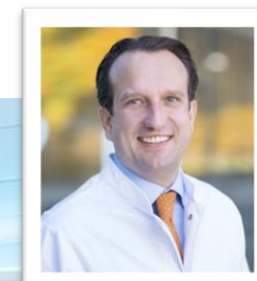
Henneberg et al. Nat Commun 2021

Treatment: correlation
effectiveness / signal

To the clinics!



In vivo an ex vivo radiotracer accumulation



Prof. La Fougère
(UKT)

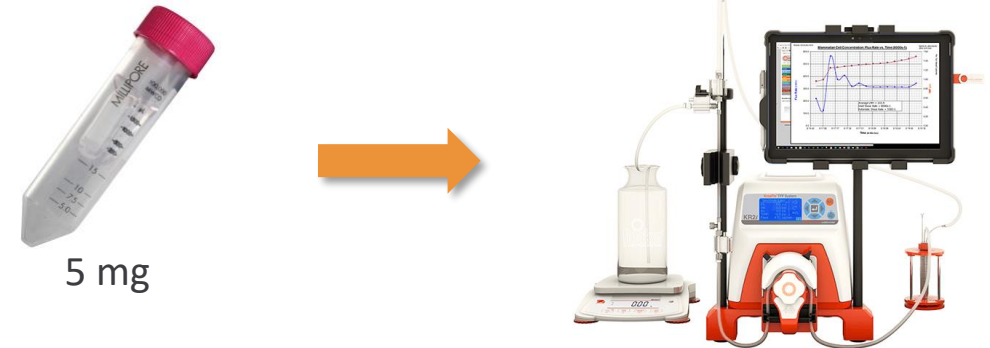
Clinical translation preparation

Tox assays:

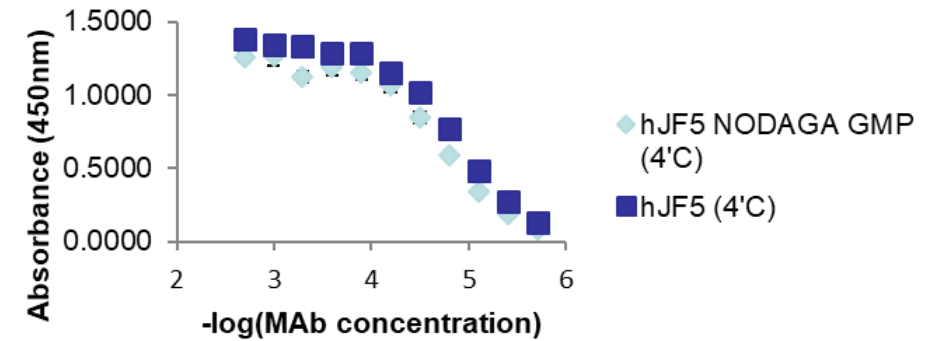


HED tested: 48,4 $\mu\text{g}/\text{kg}$
Intended human dose: 16,7 $\mu\text{g}/\text{kg}$

GMP scale-up



hJF5 PTA-ELISA against *Aspergillus* antigen



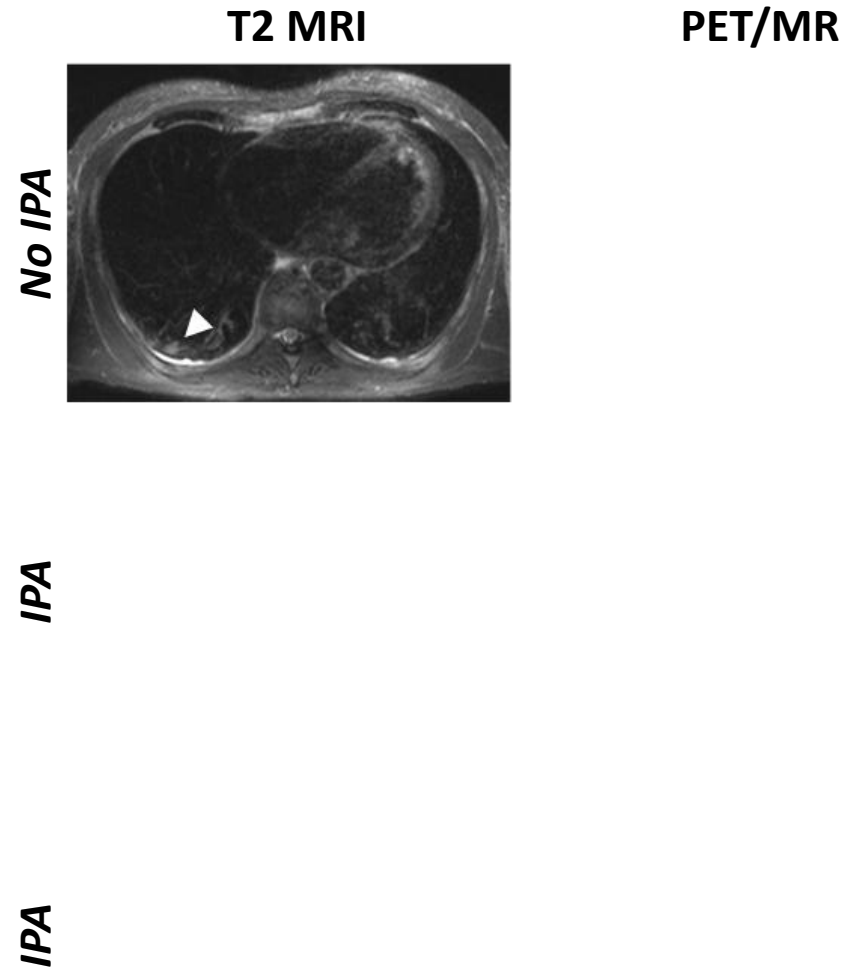
Production requirements met

First hJF5-PET clinical results

Compassionate use cases (AMG-§13.2b)

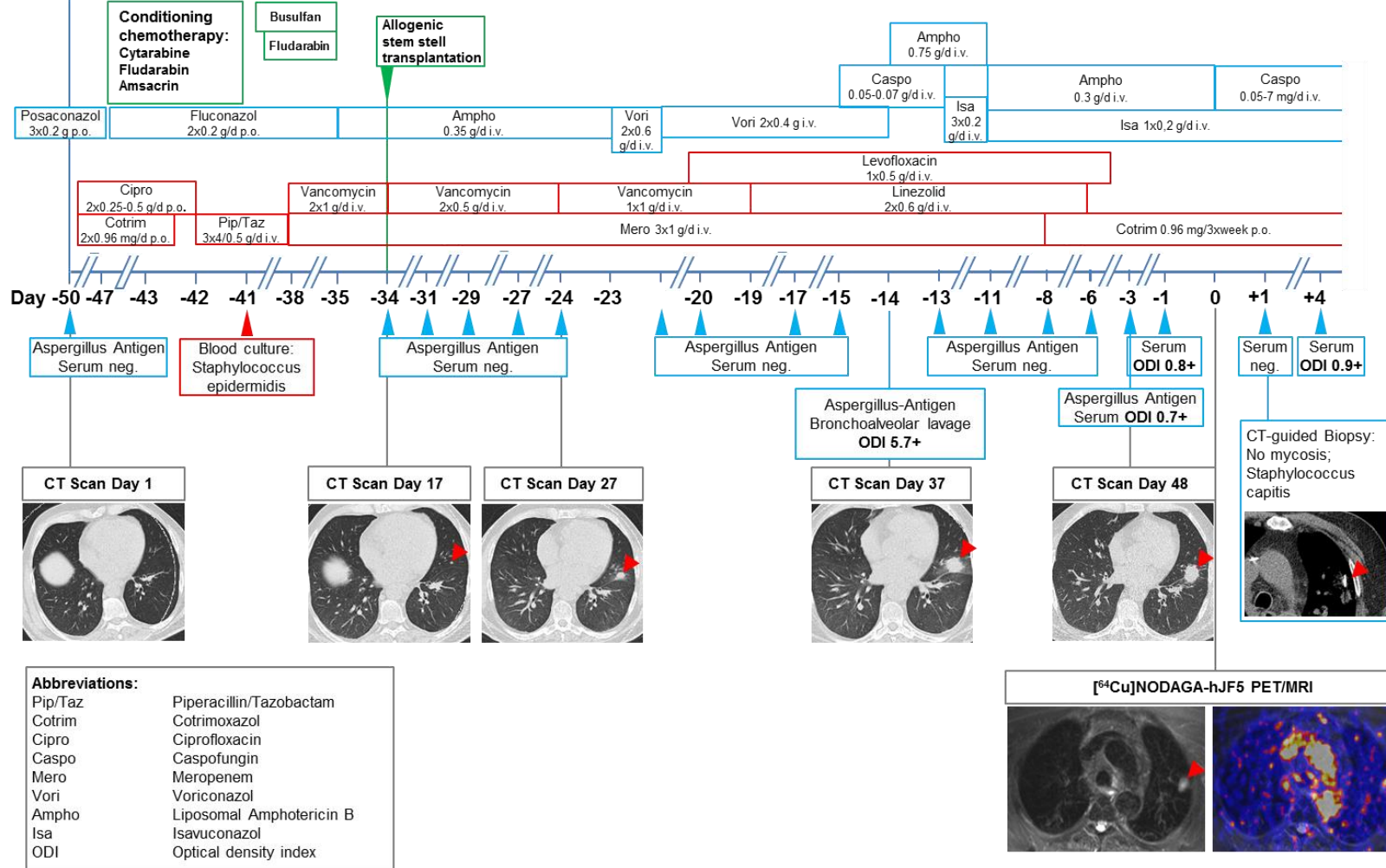
- Akute Myeloid Leukemia
 - Fever of unknown origin
 - Refractory to antibiotics
 - Non-conclusive CT
 - BAL/serum
- EORTC/MSG Diagnosis

Correlation:
EORTC/MSG Diagnosis -
PET/MR result



Patient 2

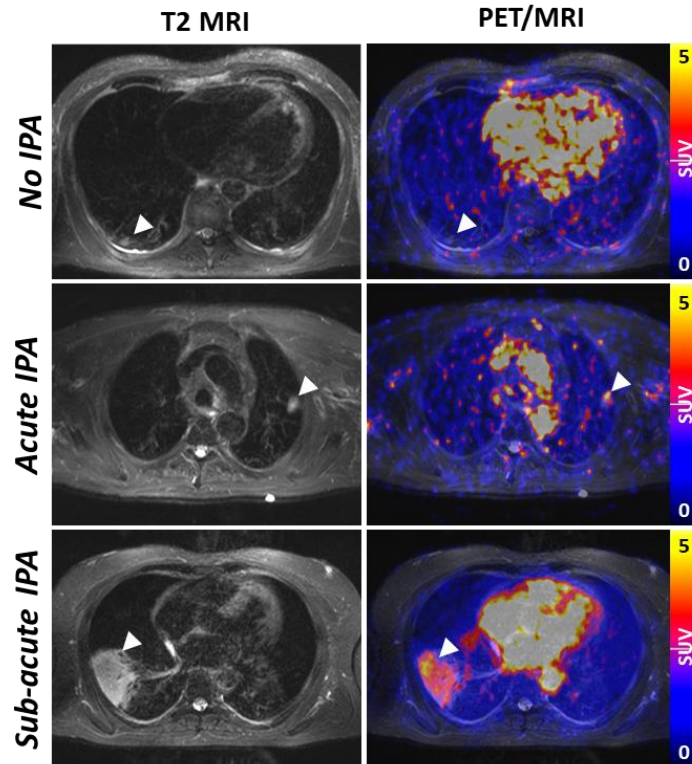
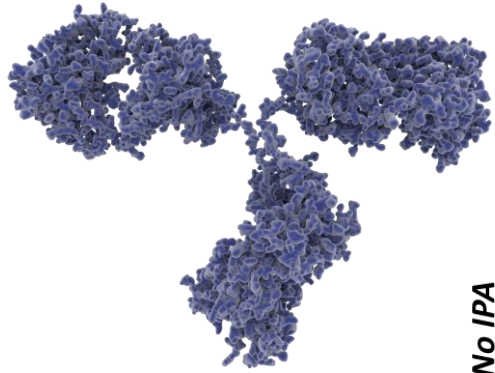
- Refractory **acute myeloid leukemia**
- Conditioning chemotherapy and allogenic stem cell transplantation



Conclusion

A new diagnosis and therapy monitoring approach: ImmunoPET

From the mAb to the clinics



A new toolbox

Applicable to other (fungal) infections. „Just“ need a proper antibody

IgG1 framework

Extensive circulation time

- Extends radiation exposure
- Requires 1+day of uptake time before scan
- High background (blood) signal

➔ Antibody derivatives?

Acknowledgments



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WSS

WERNER SIEMENS-STIFTUNG

Thank you all for your attention!
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