



# Preclinical Imaging @ Tübingen

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# New Radiopharmacy



# Our Facility





# Sham vs. Therapy: PI3K



days p.o. 16

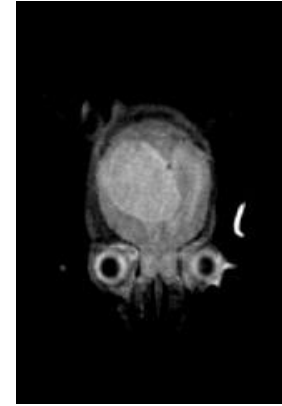
20

23

27

30

M24 Sham



days p.o. 16

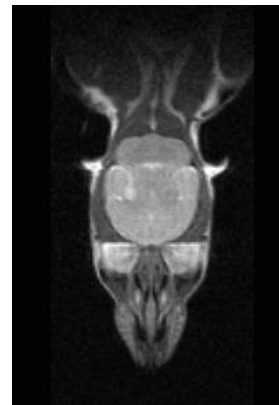
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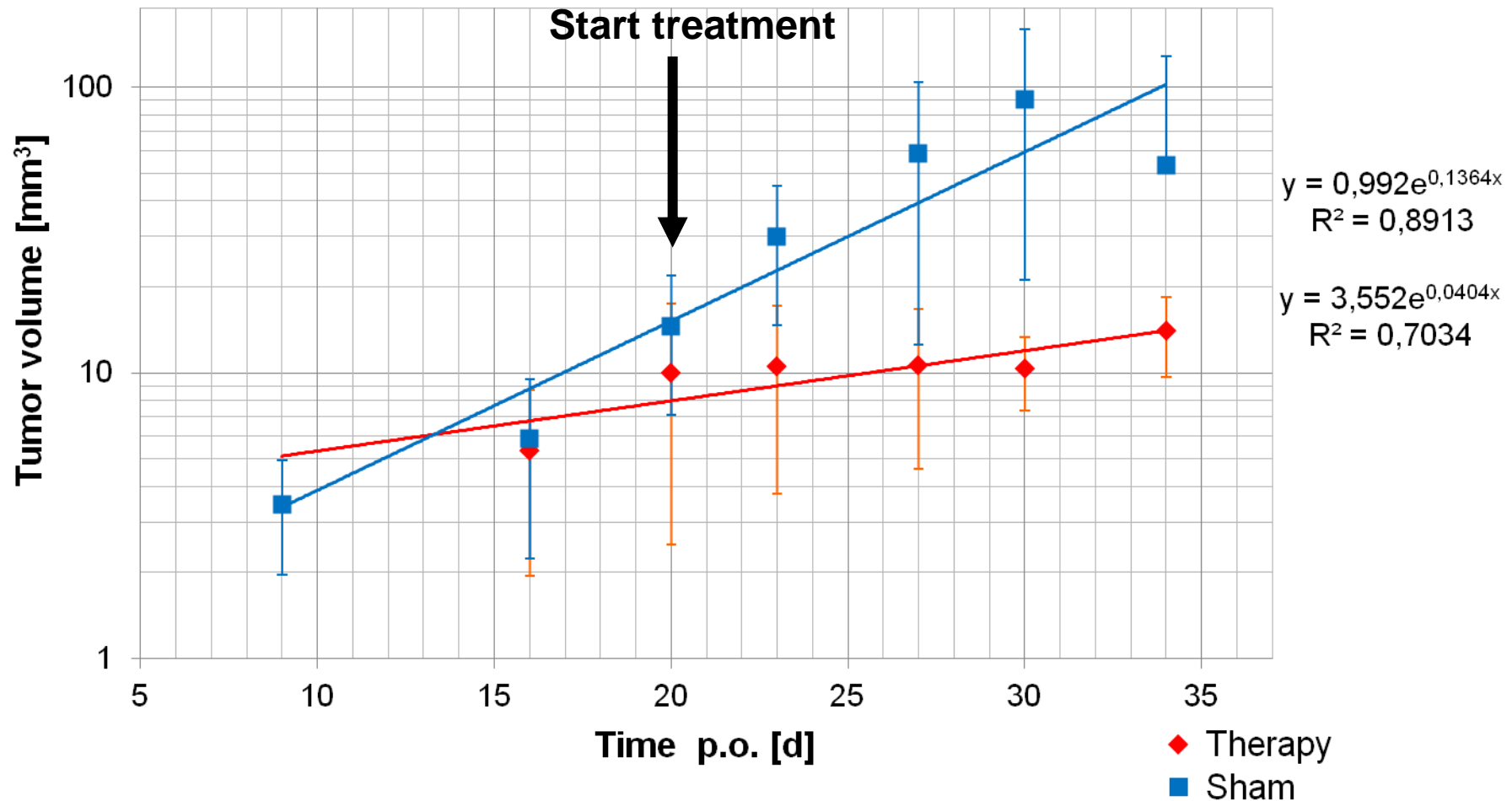
27

30

M09 Therapy



# Tumor growth: Sham vs. Therapy



$$Y = A * e^{Bx}$$

T-test → B (Sham) vs. B (Therapy): **P = 0.00009**

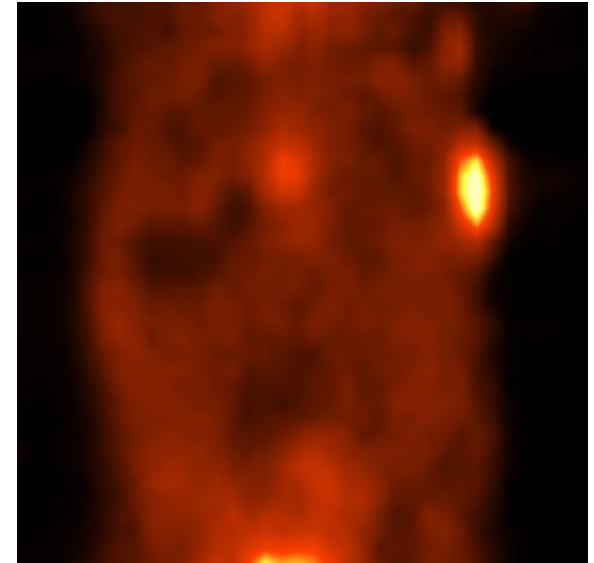
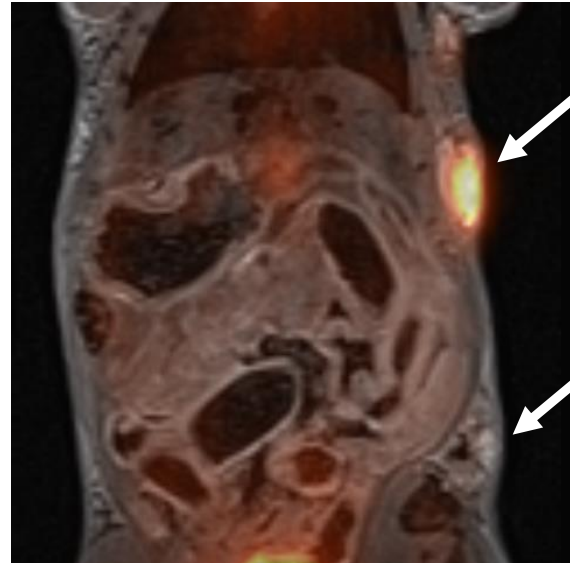
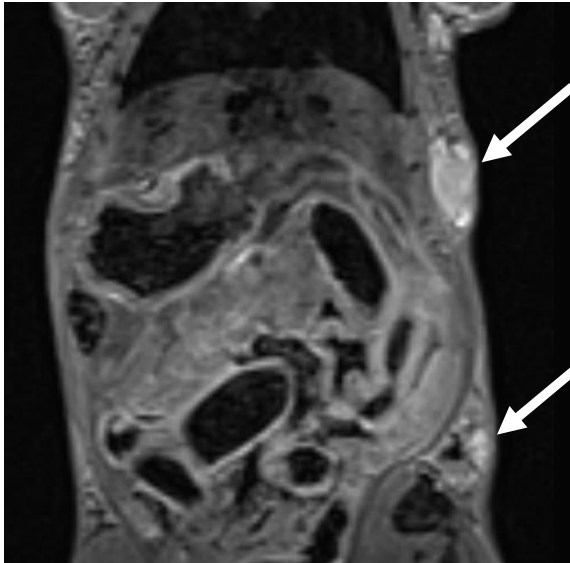
## MRI

- high resolution
- high soft tissue contrast

+

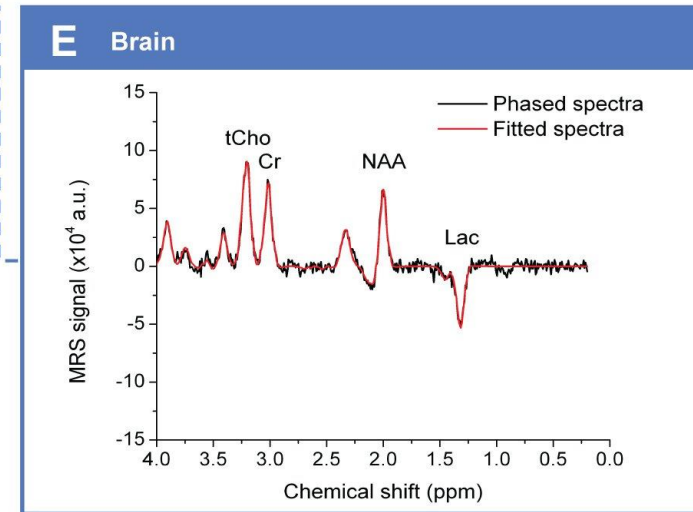
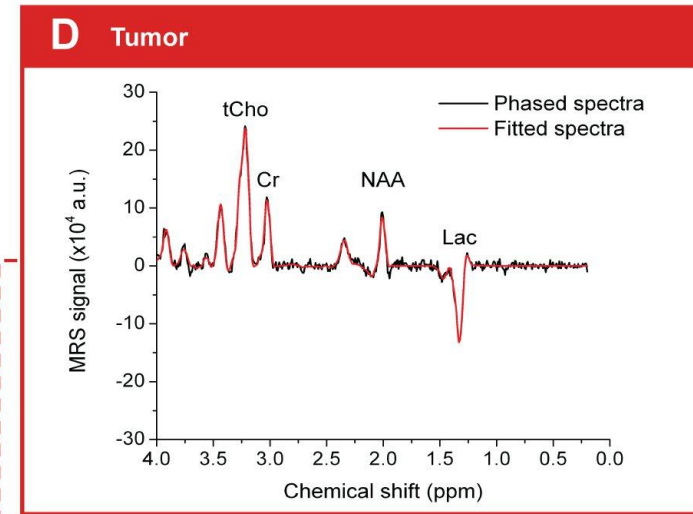
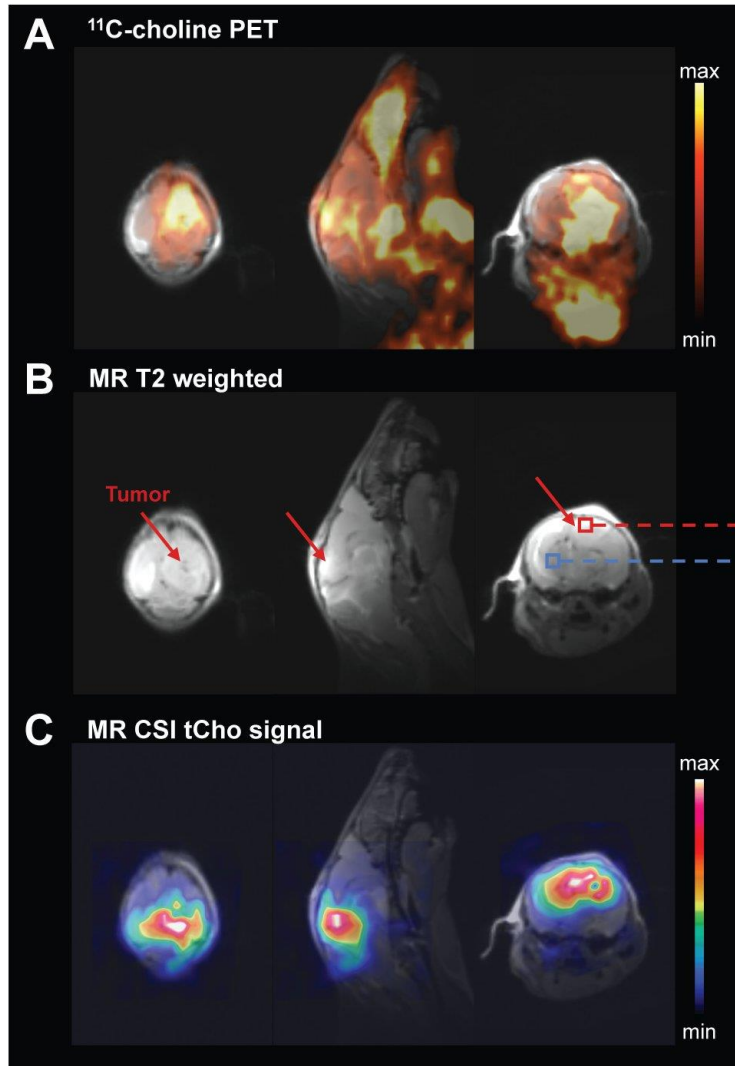
## PET

- high sensitivity
- target specific tracer



Added value by PET/MRI

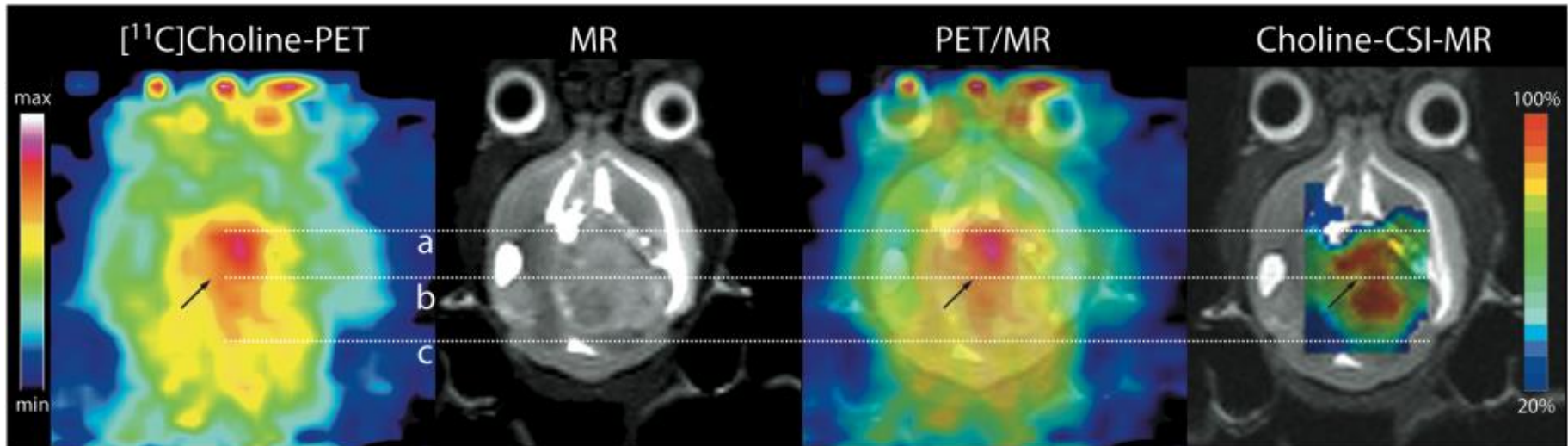
A. Schmid, et al.; *Mol Im Biol*; 2012



H.F. Wehrl, et al.; *Cancer Research*; 2013



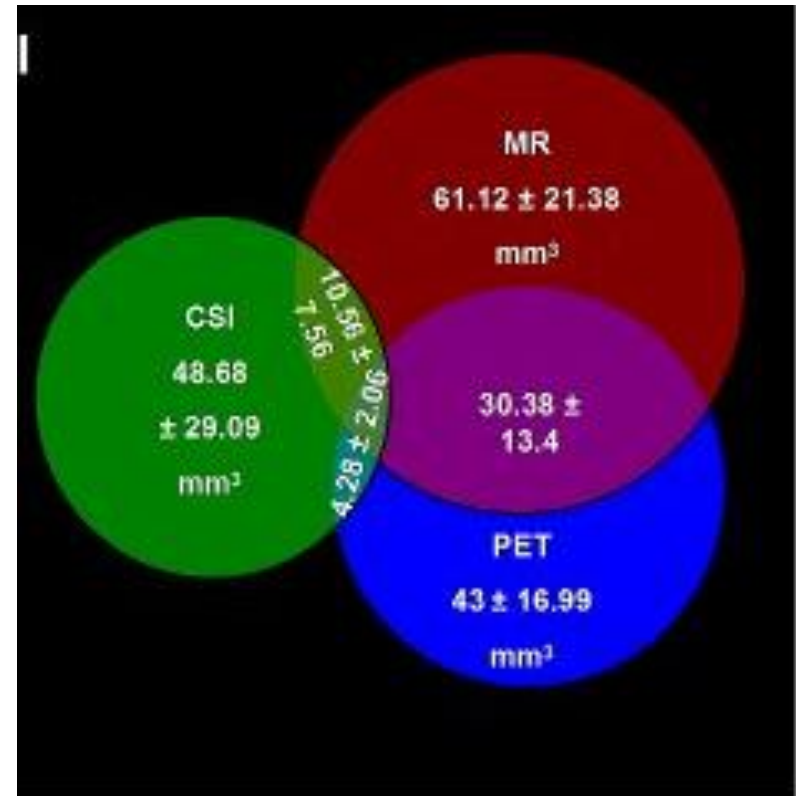
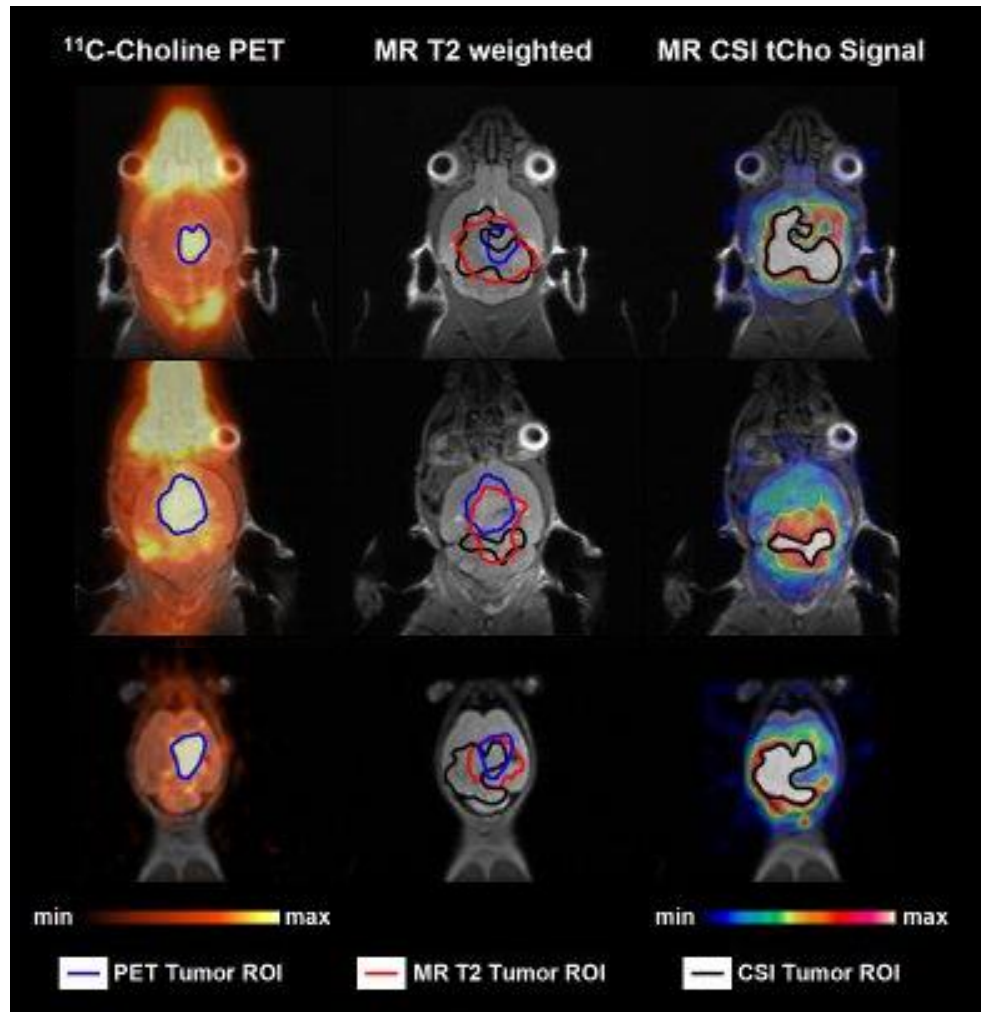
- PET/MR-spectroscopy and [ $^{11}\text{C}$ ]Choline-Tracer administration in VMDk mouse with brain tumor
- [ $^{11}\text{C}$ ]Choline PET versus CSI (tCh)



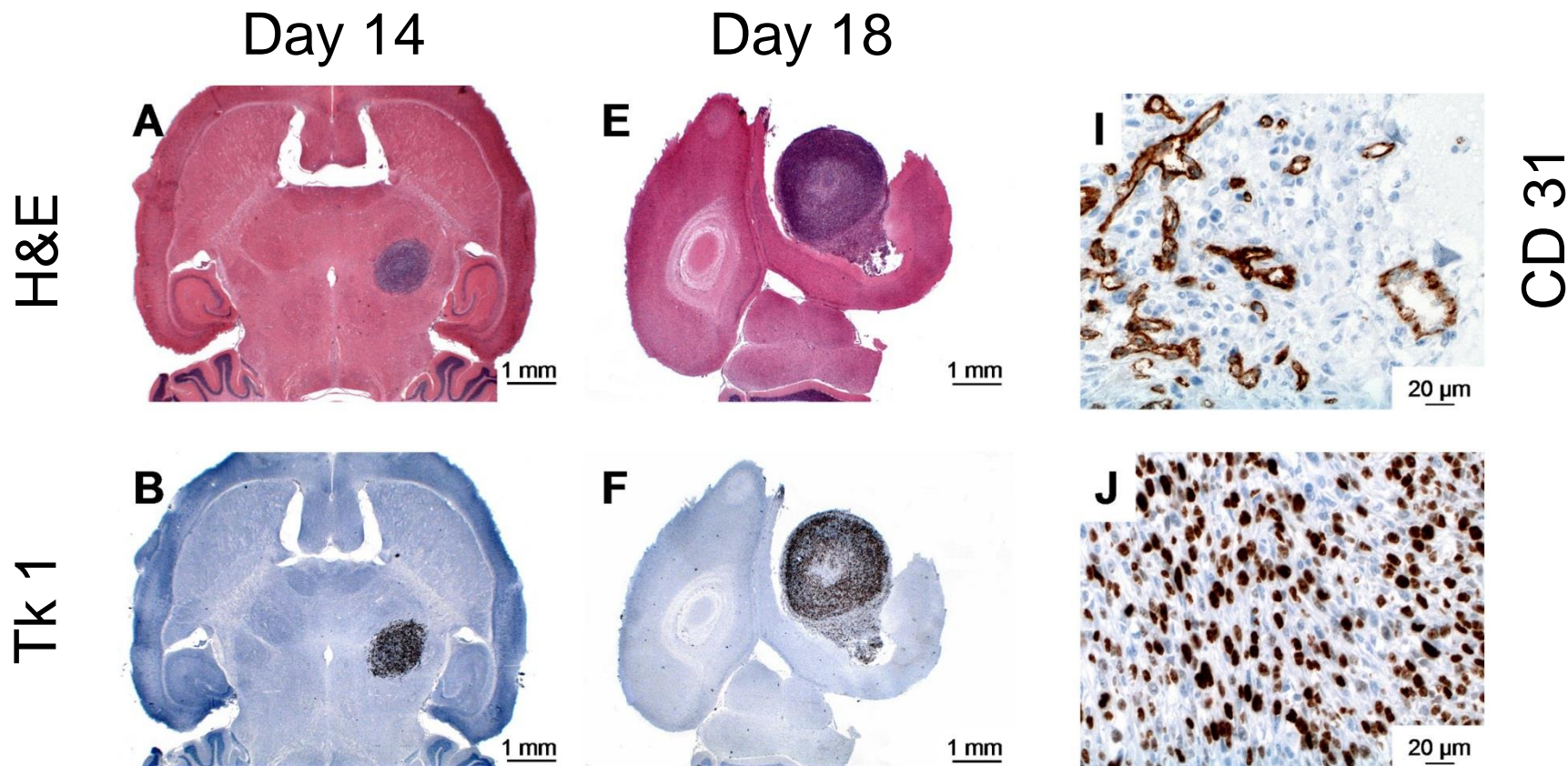
- spatial extent does not quite well match (dotted lines)
- differentiation between carcinoma *in situ*/hyperplasia/solid tumor?
- maxima do not match

possibility for complimentary information (high Cho metabolic rate vs. deposited choline)

H.F. Wehrl, et al.; **Cancer Research**; 2013



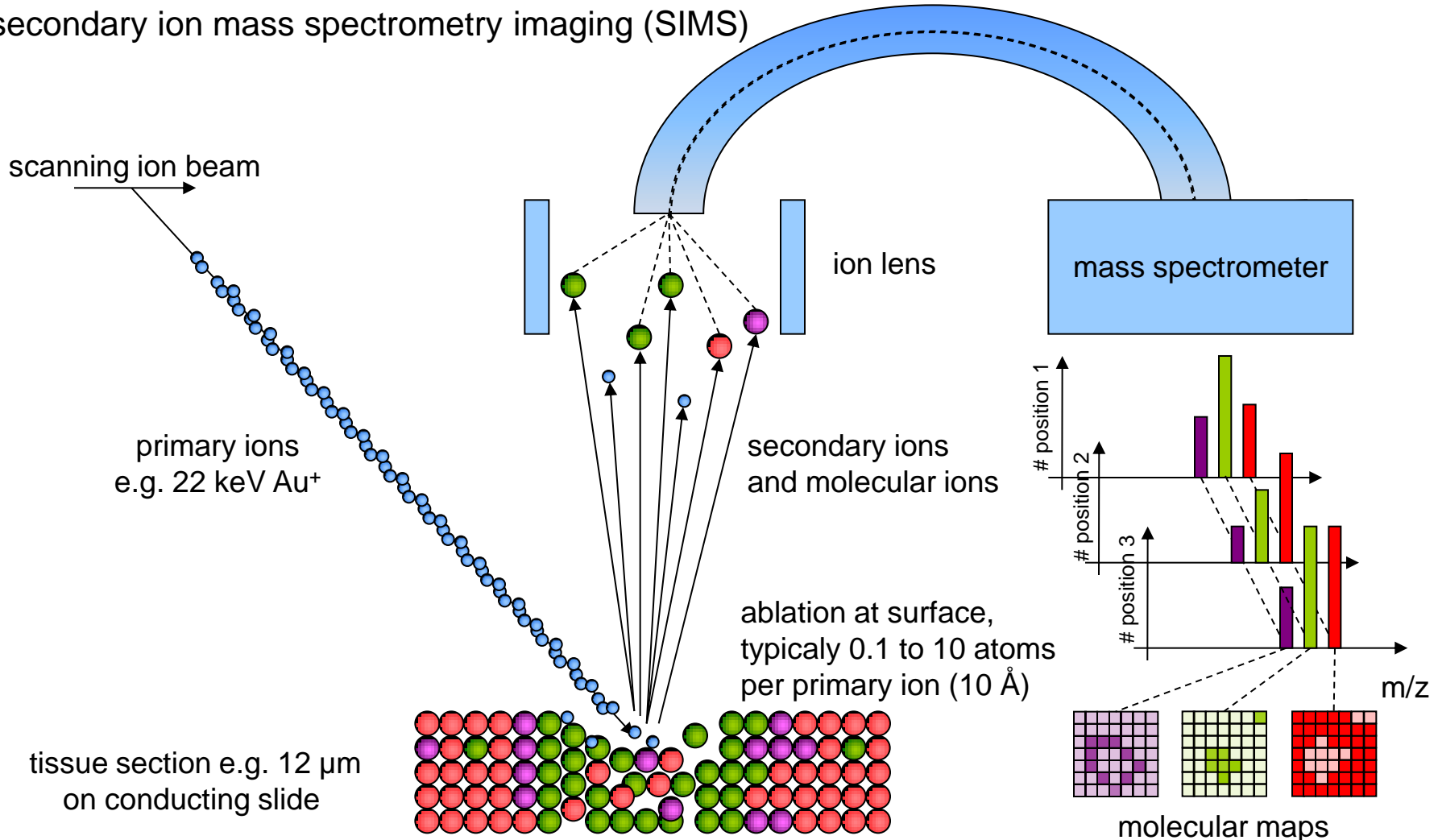
H.F. Wehrl, et al.; **Cancer Research**; 2013

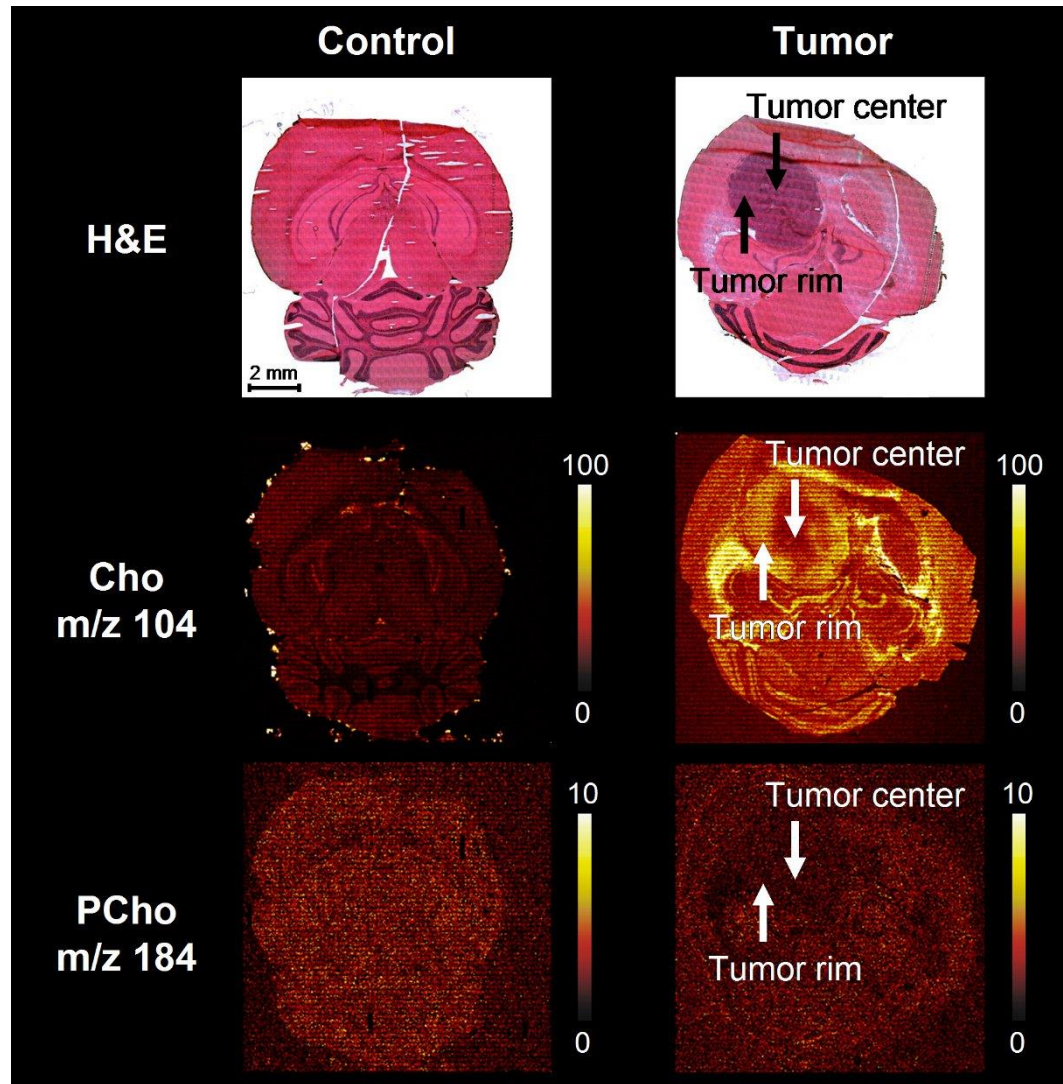


H.F. Wehrl, et al.; *Cancer Research*; 2013

# Choline Metabolism studied by PET/MR

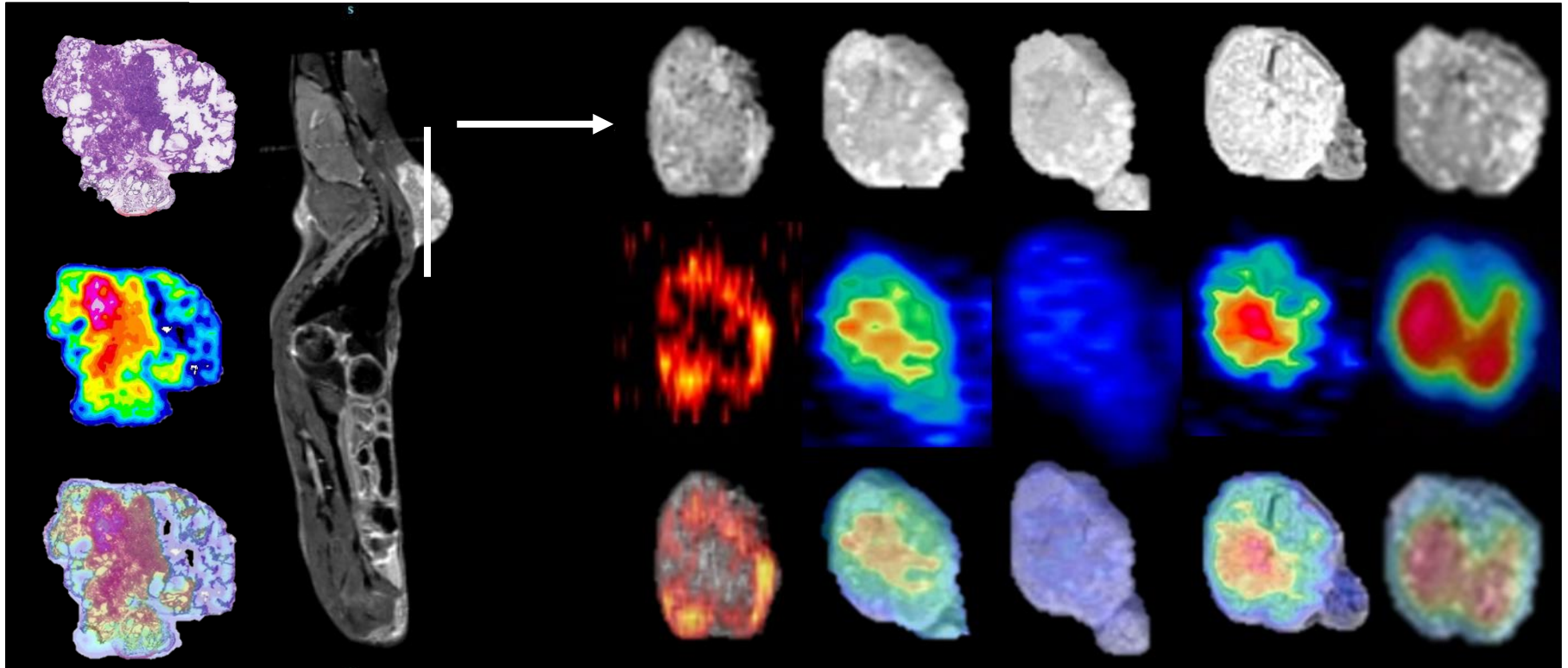
- **ex vivo correlation needed:** Histology and SIMS
- secondary ion mass spectrometry imaging (SIMS)

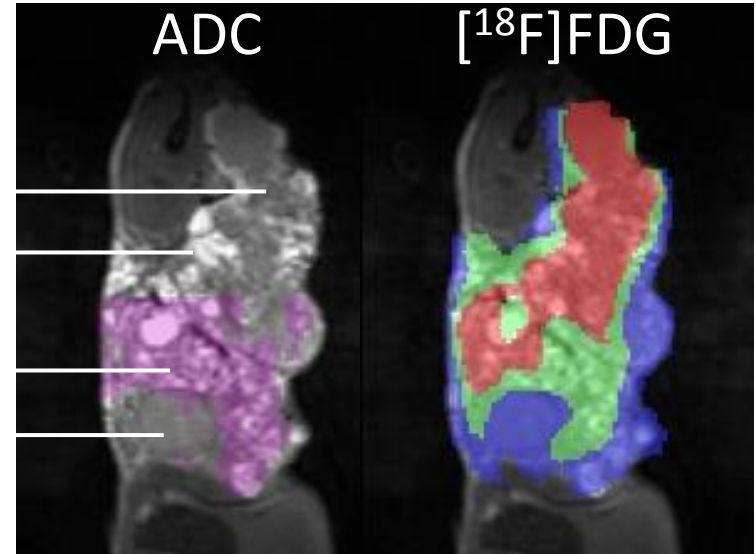
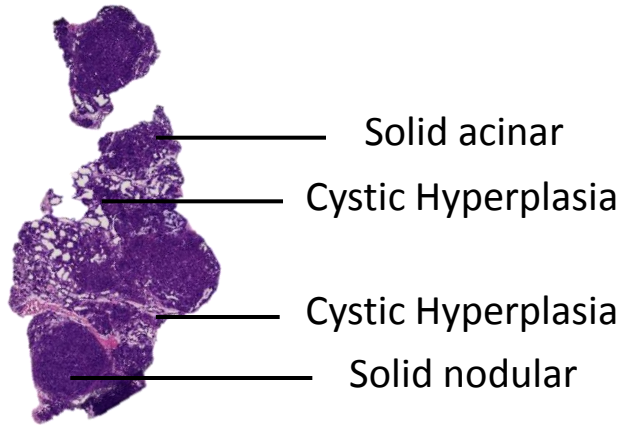
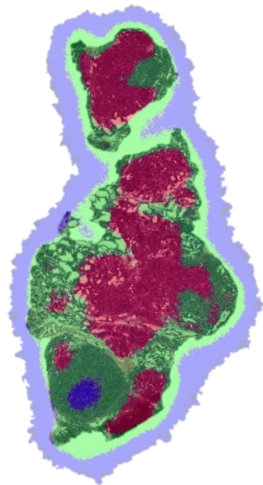




H.F. Wehrl, et al.; **Cancer Research**; 2013

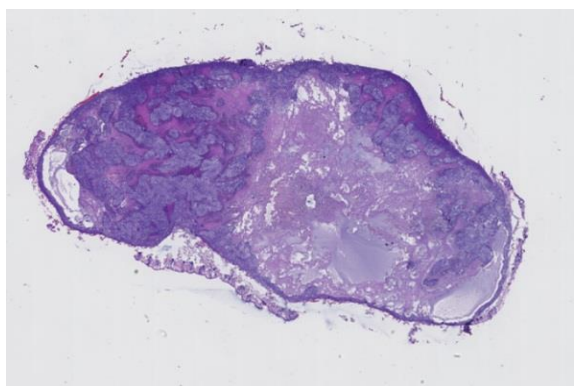
	ADC	[ <sup>68</sup> Ga]	[ <sup>18</sup> F]	[ <sup>11</sup> C]	[ <sup>18</sup> F]
Tumor volume [mm <sup>3</sup> ]	[10 <sup>-6</sup> mm <sup>2</sup> /s]	RGD	FMISO	Chol	FDG
mean SUV [418.7]	665.3	0.14	0.45	0.65	1.26
hotspots SUV	1712.2	0.23	0.62	1.43	2.48



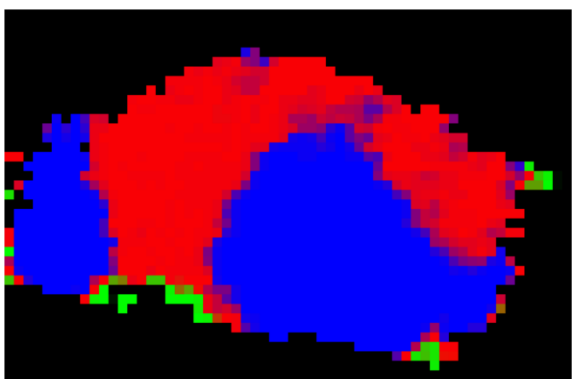


■  $[^{18}\text{F}]\text{FDG} < 3.9 \text{ TMR}$     
 ■  $[^{18}\text{F}]\text{FDG} 3.9 - 9.1 \text{ TMR}$     
 ■  $[^{18}\text{F}]\text{FDG} > 9.1 \text{ TMR}$     
 ■  $\text{ADC} > 1009 \cdot 10^{-6} \text{ mm}^2/\text{s}$

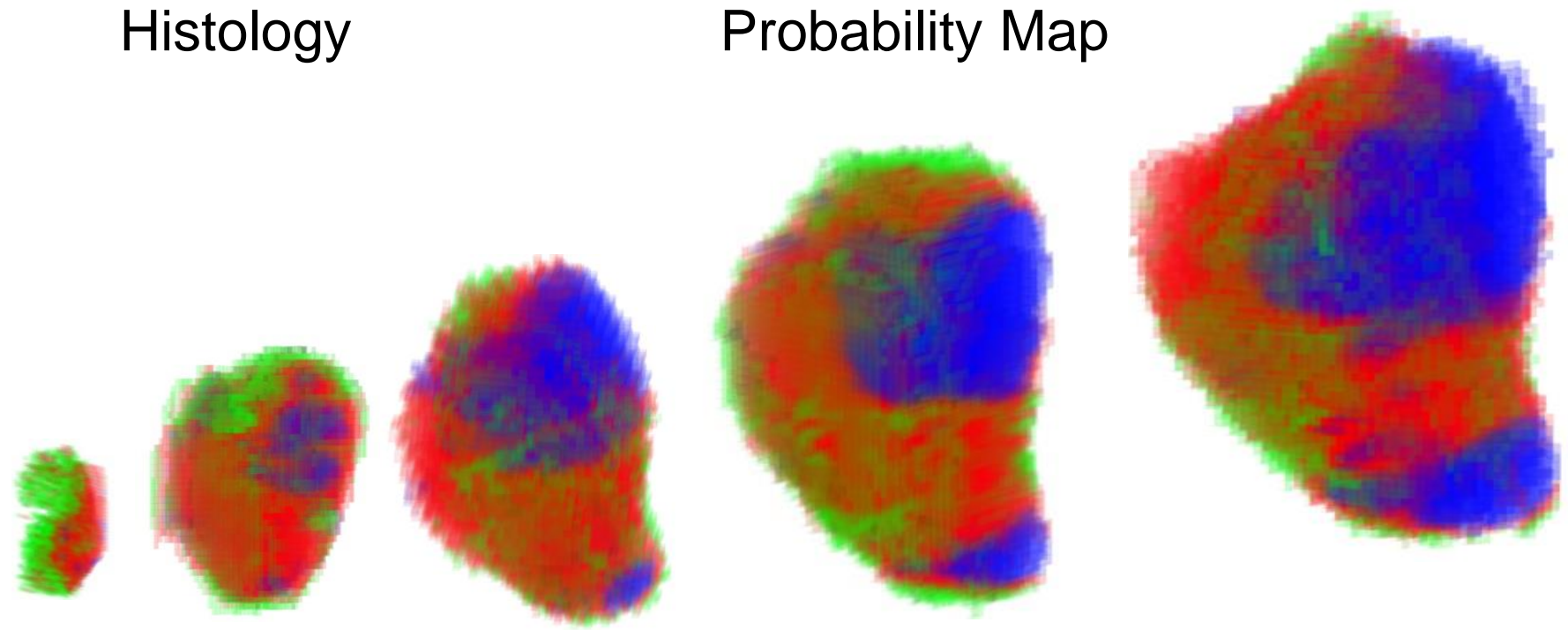
Population	$[^{18}\text{F}]\text{FDG}$	ADC
solid nodular	-	-
cystic hyperplasia	-/+	+
solid acinar	++	-



Histology



Probability Map







# Metastasis & Premetastatic Niche

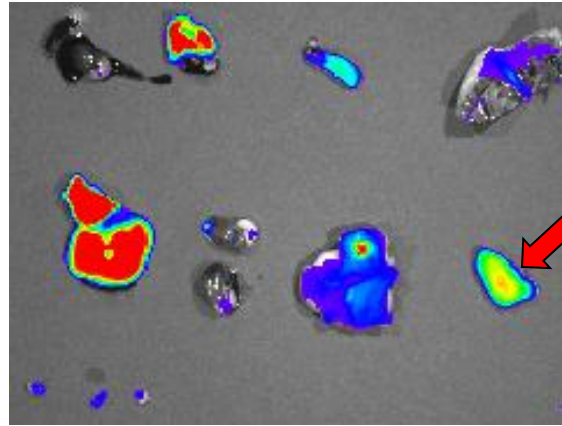
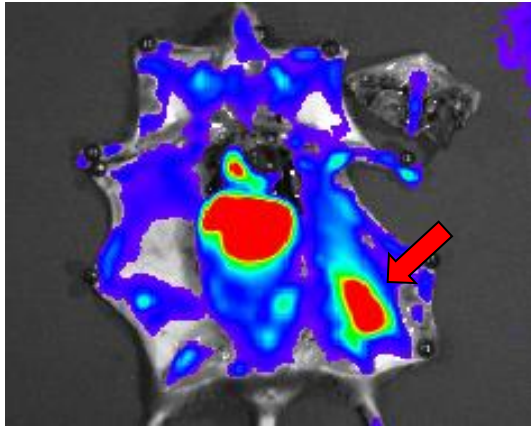
- Simultaneous tracking of Cy5-G-MDSC and Luciferase-tumorcells
  - intracardiac injection
  - orthotopic injection (mammary fat pad)
  - i.v. injection

G-MDSC: Granulocyte myeloid-derived suppressor cells

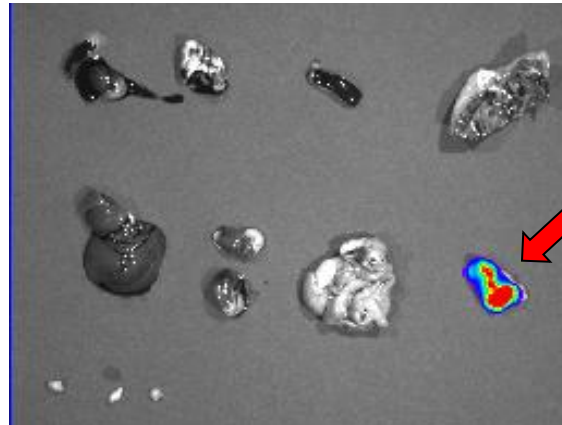
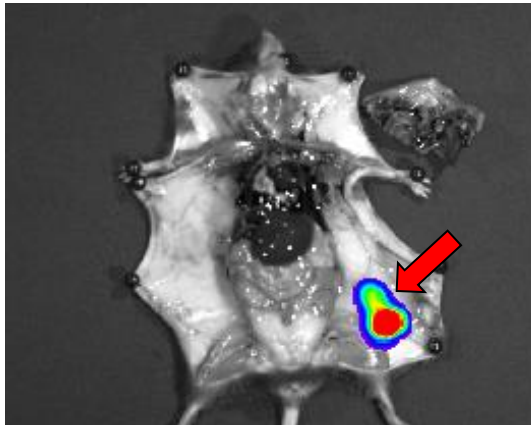
“Butterfly”

Organs

FL



BL



**G-MDSC  
systemic**

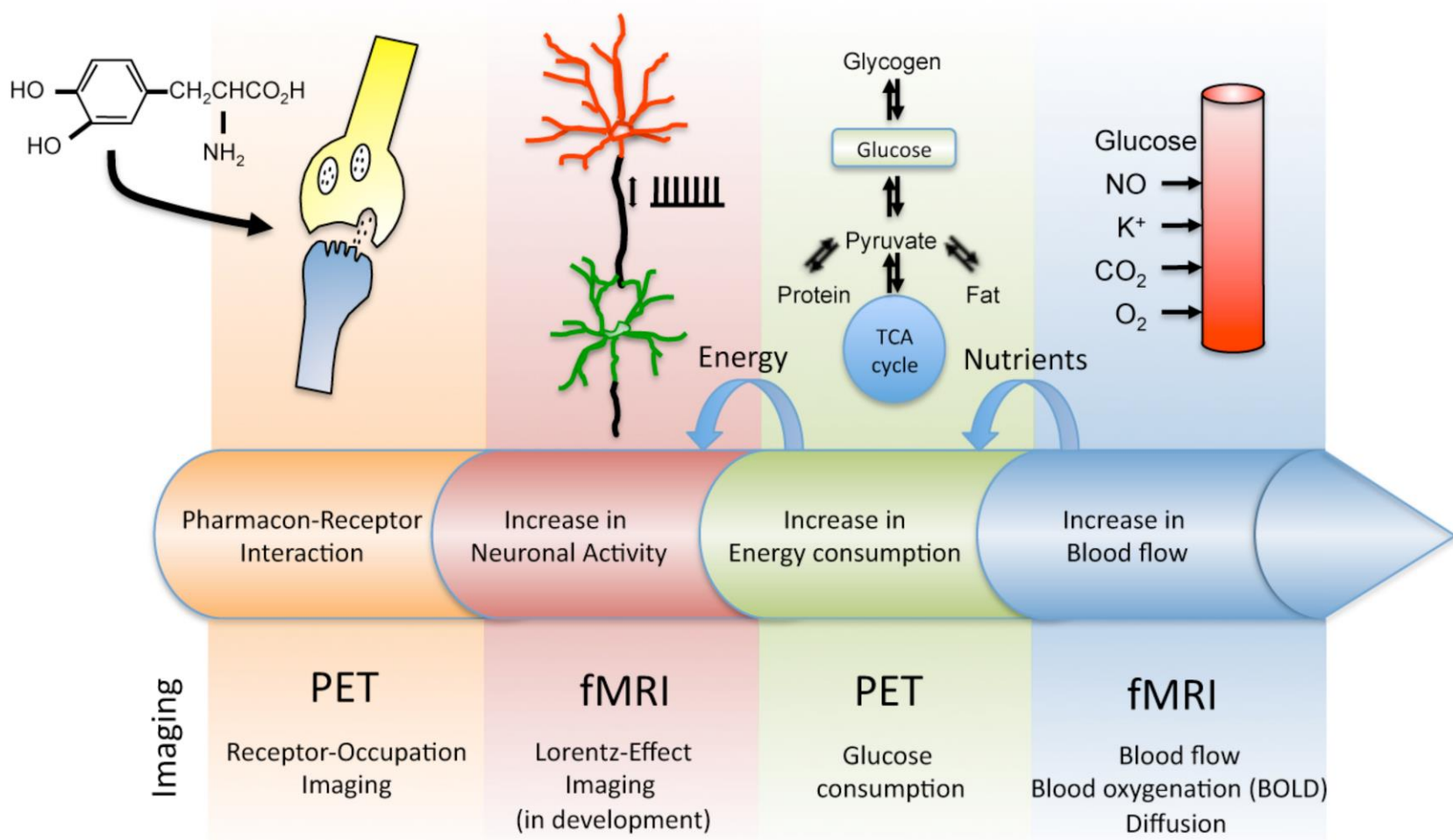
**Tumor cells  
MMFP**

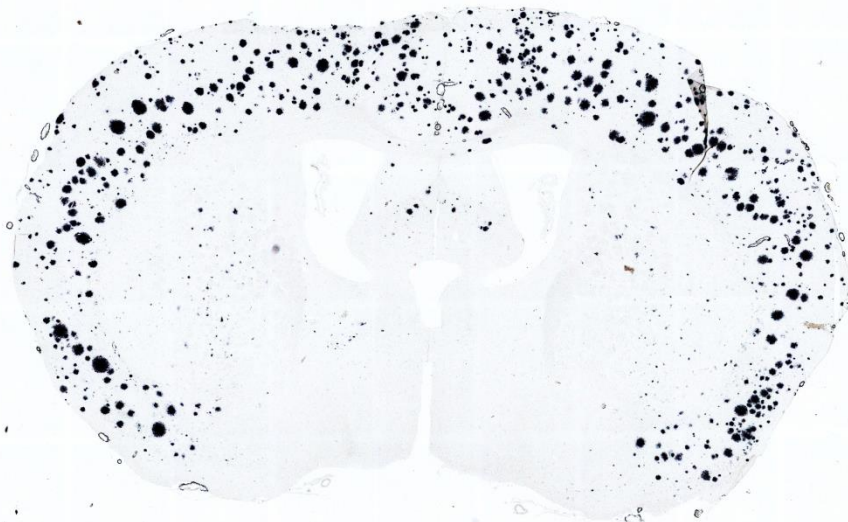


# PET/MR in Neuro Research

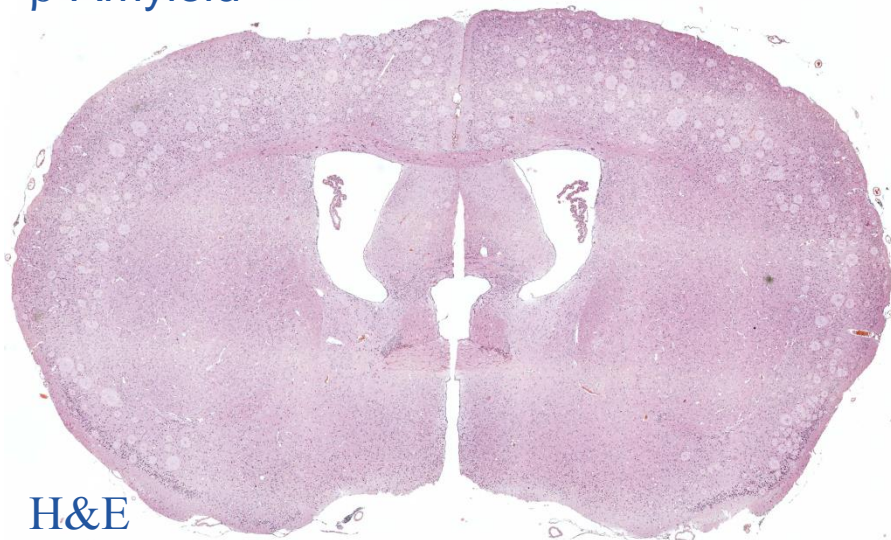
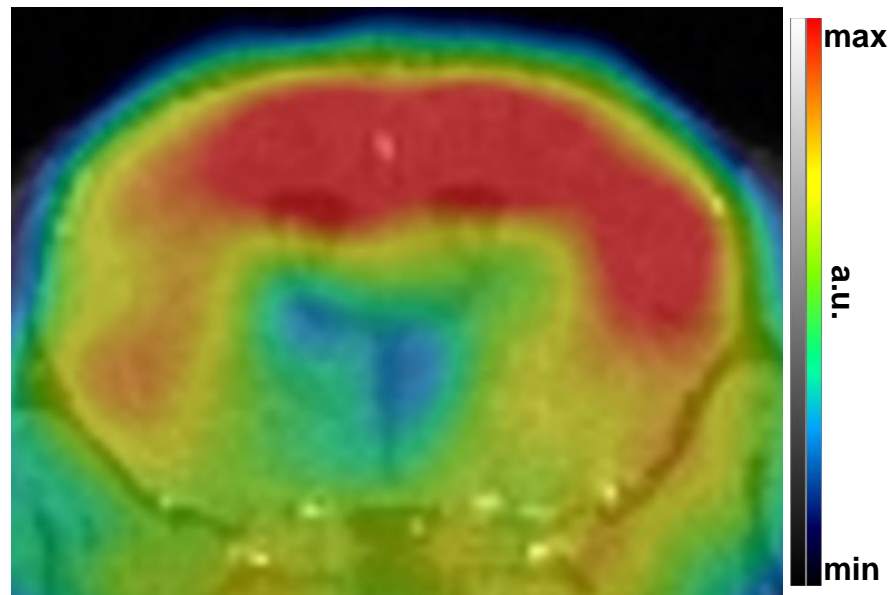


# Brain Function as a Result of Receptor Activation

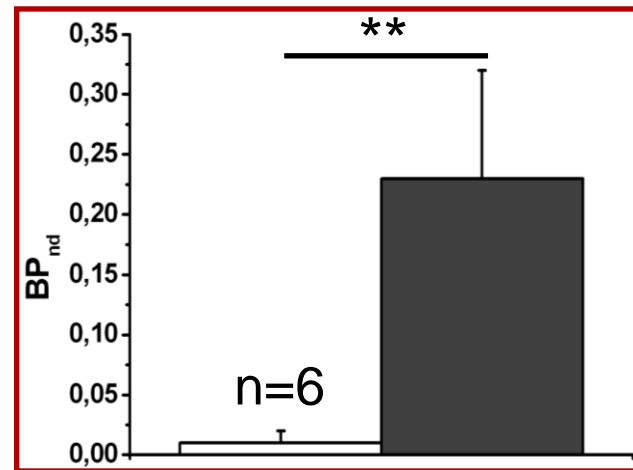


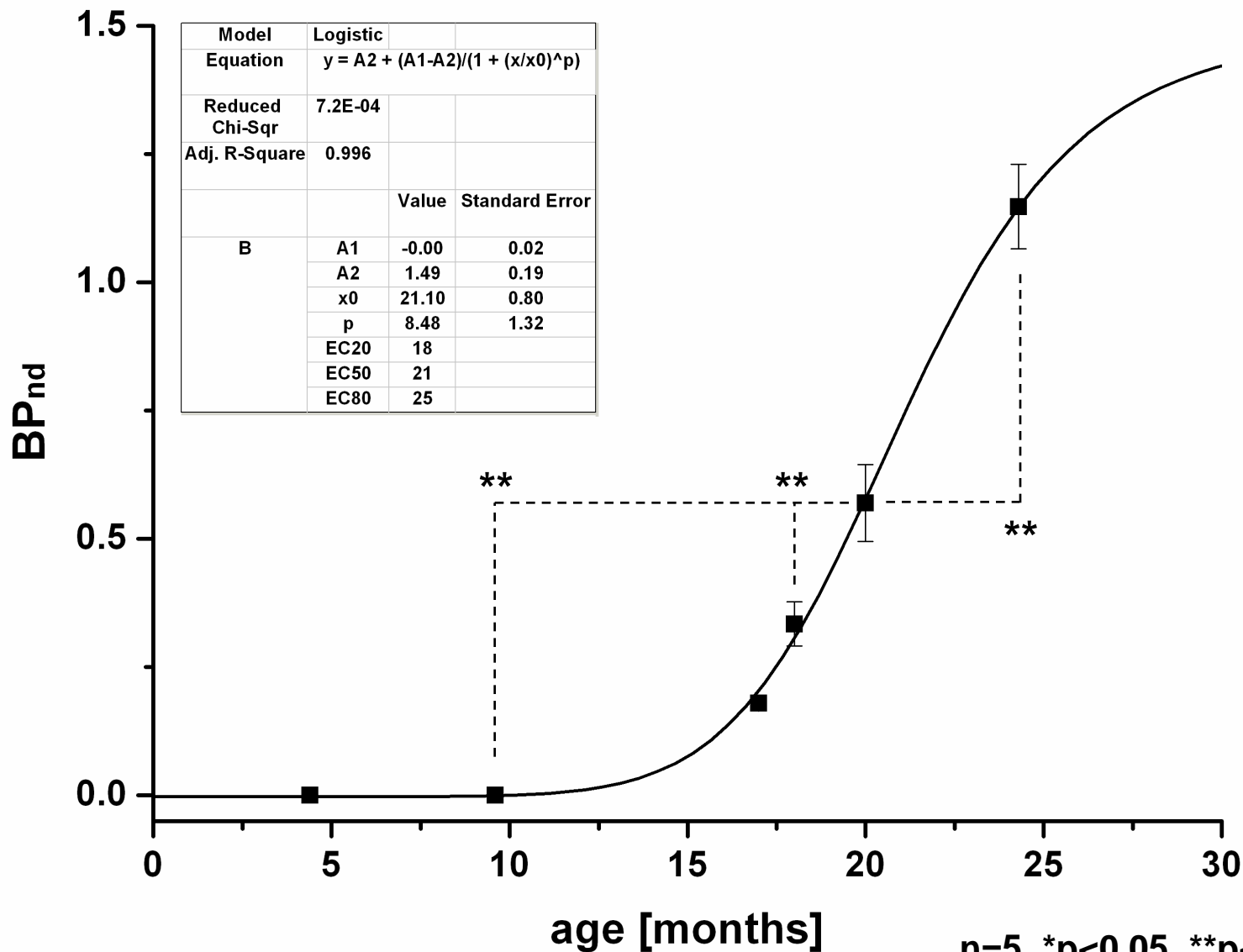


$\beta$ -Amyloid

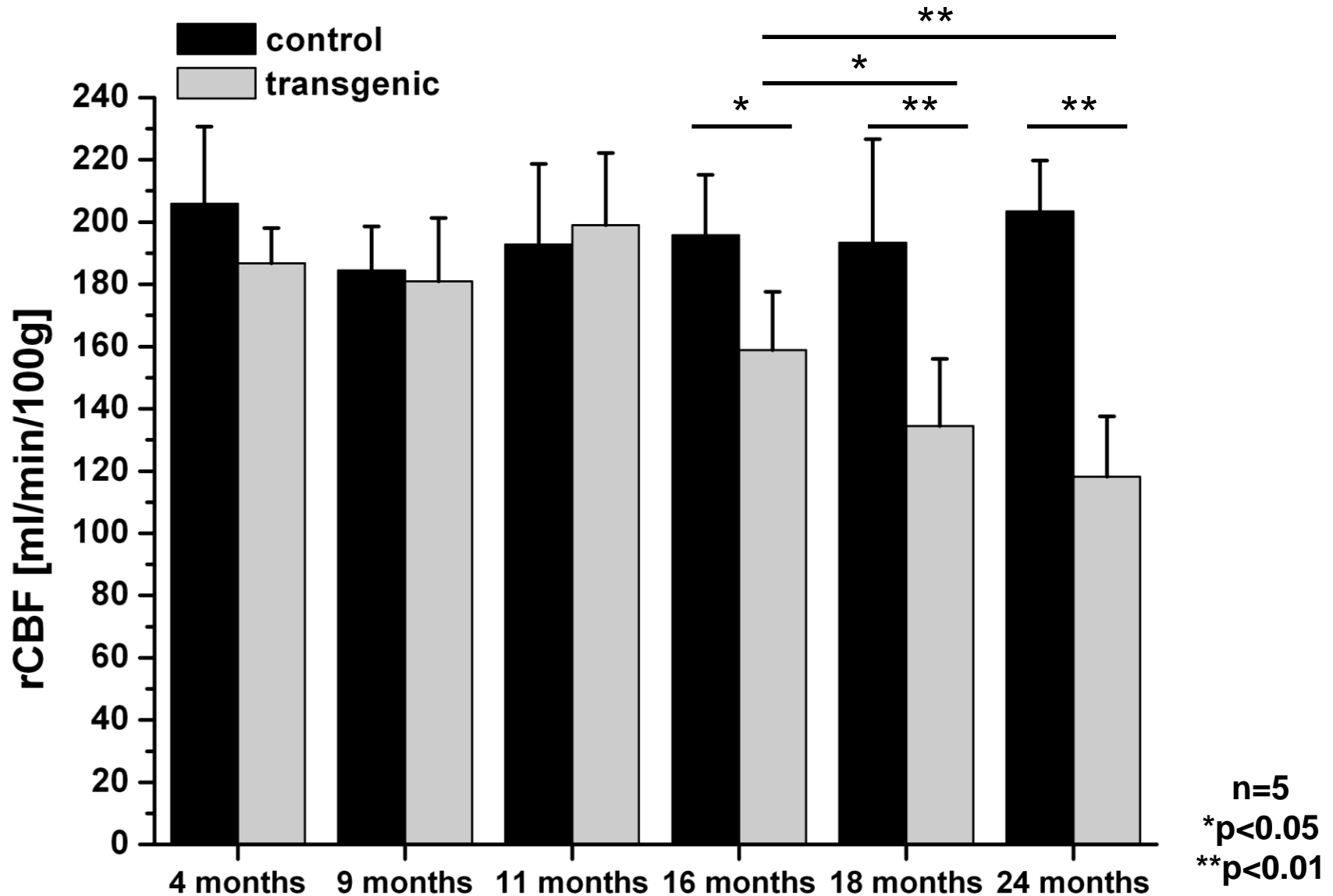


H&E





n=5, \*p<0.05, \*\*p<0.01





# Targeting Aspergillus Infection: Diagnosis & Treatment

The approach of the consortium is to develop new **disease specific tracers** based on **monoclonal antibodies** along with **molecular imaging technologies PET/MR** and **microscopy**.

Newly developed tracers shall then be functionalised by a combined labelling with radio-isotopes allowing diagnostic PET imaging but also **radio-immunotherapy**, thus representing truly anti-infectious theranostics.

This would provide a framework for new tools in the management not only of this **rare** but **life-threatening mycosis** but principally also for other infectious hazards.

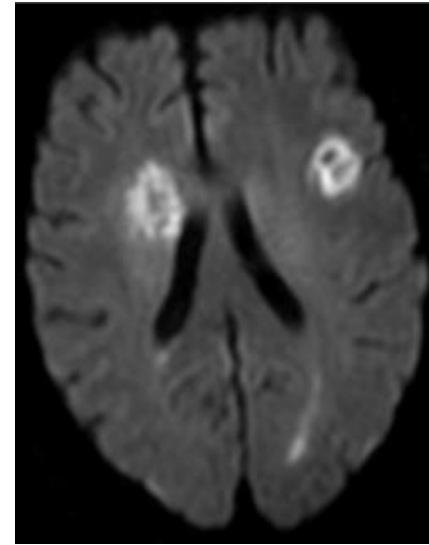
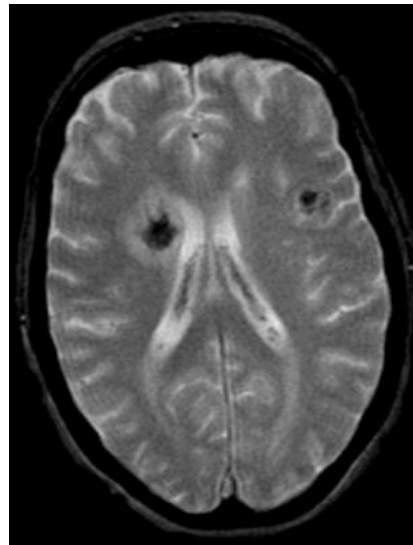
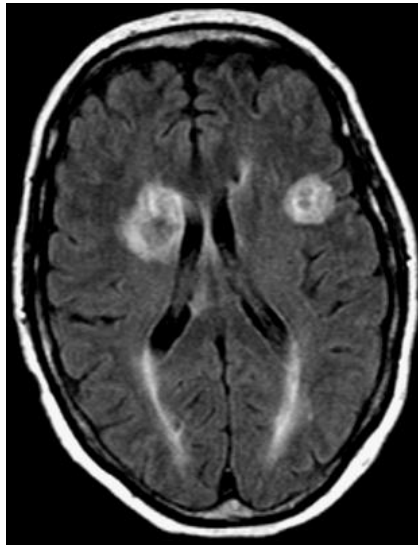
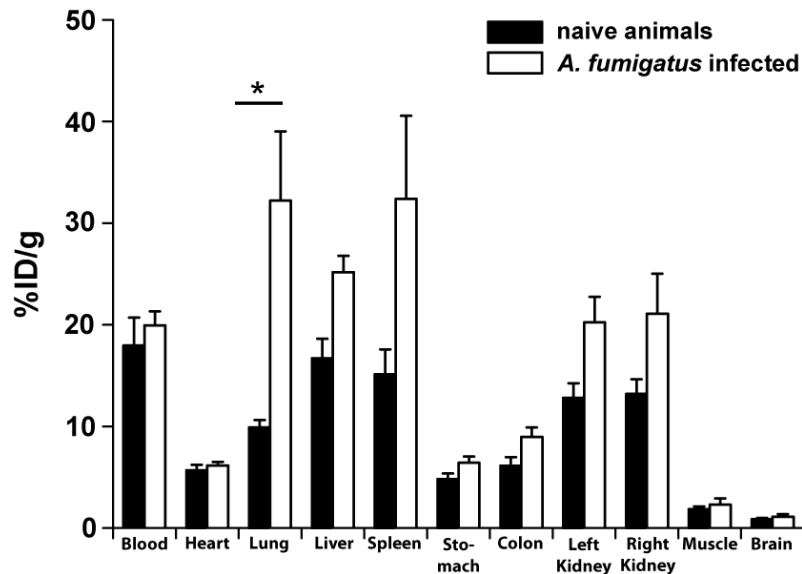
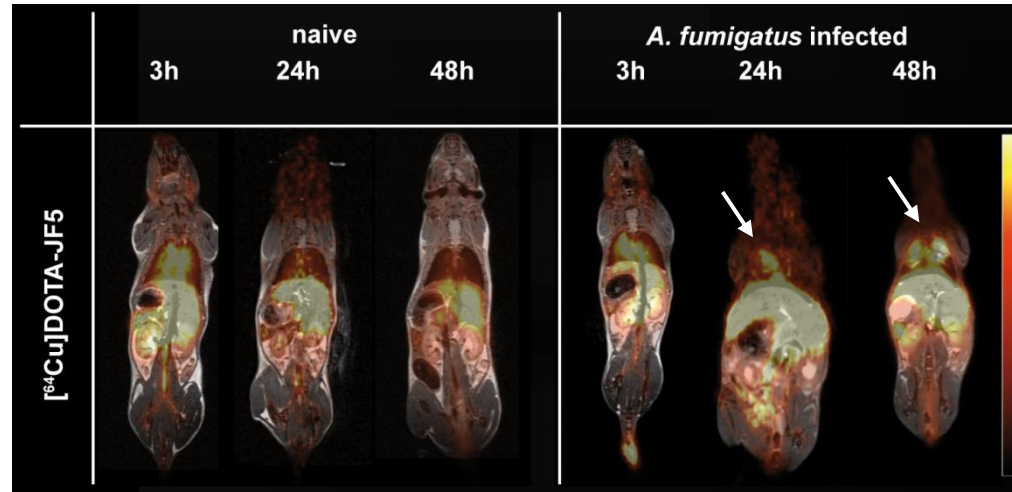


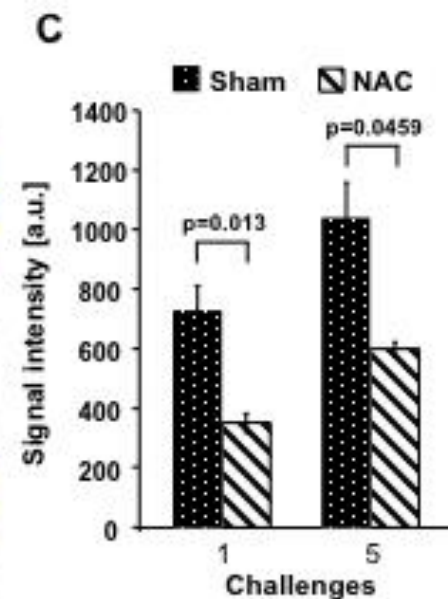
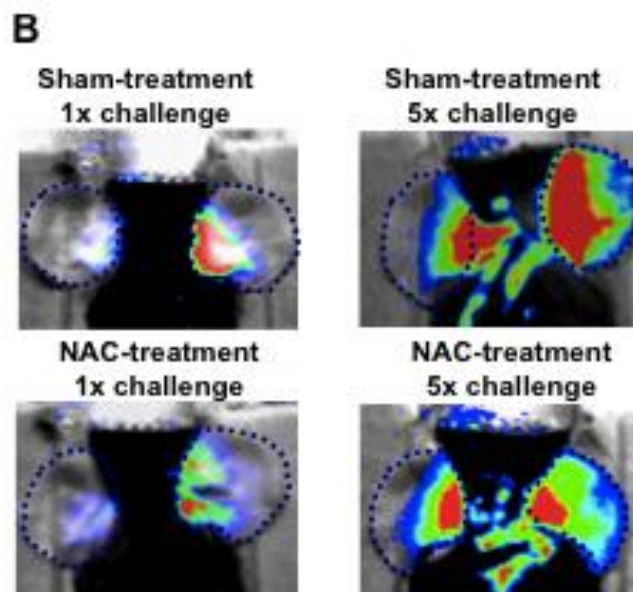
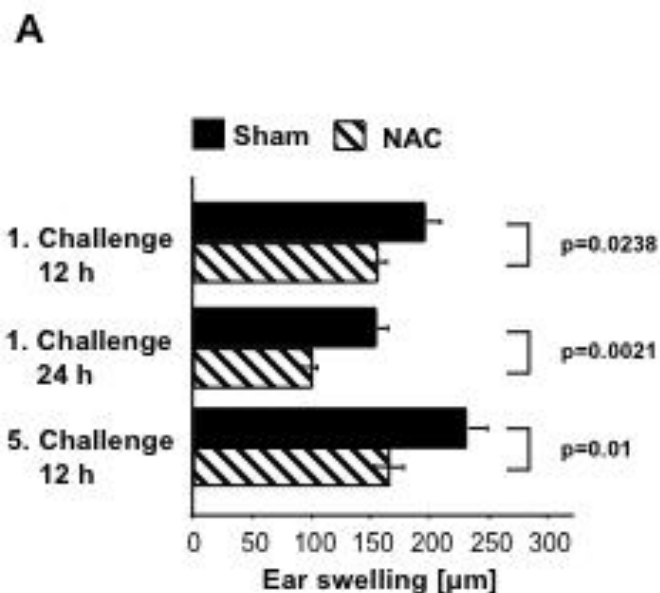
Image Courtesy: Prof Ernemann, Prof Nägele  
Neuroradiology Tübingen

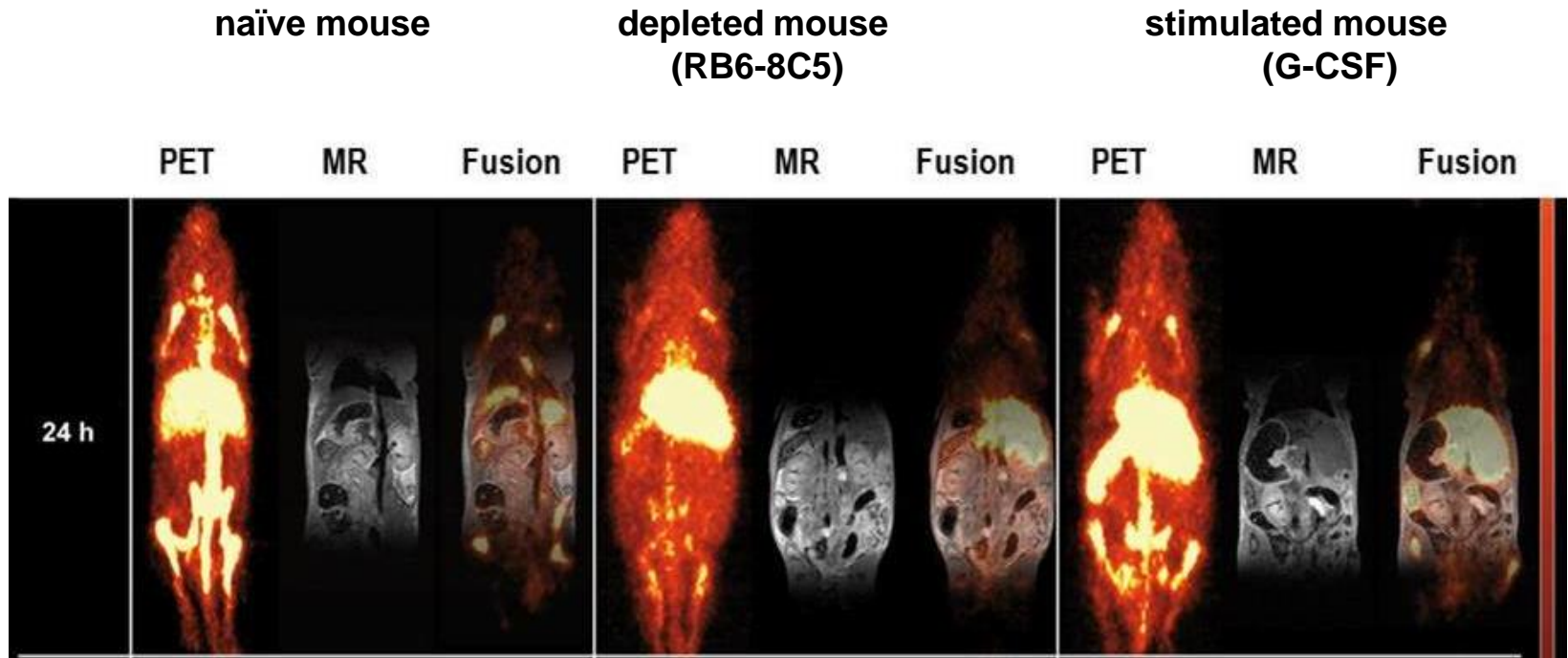
- **Invasive Aspergillosis**

- *A. fumigatus* most prevalent airborne fungal pathogen
- size of conidia: 2-3  $\mu\text{m}$   $\rightarrow$  ability to reach lung alveoli
- major cause of infectious morbidity and mortality in immunocompromised patients
- bone marrow and organ transplants



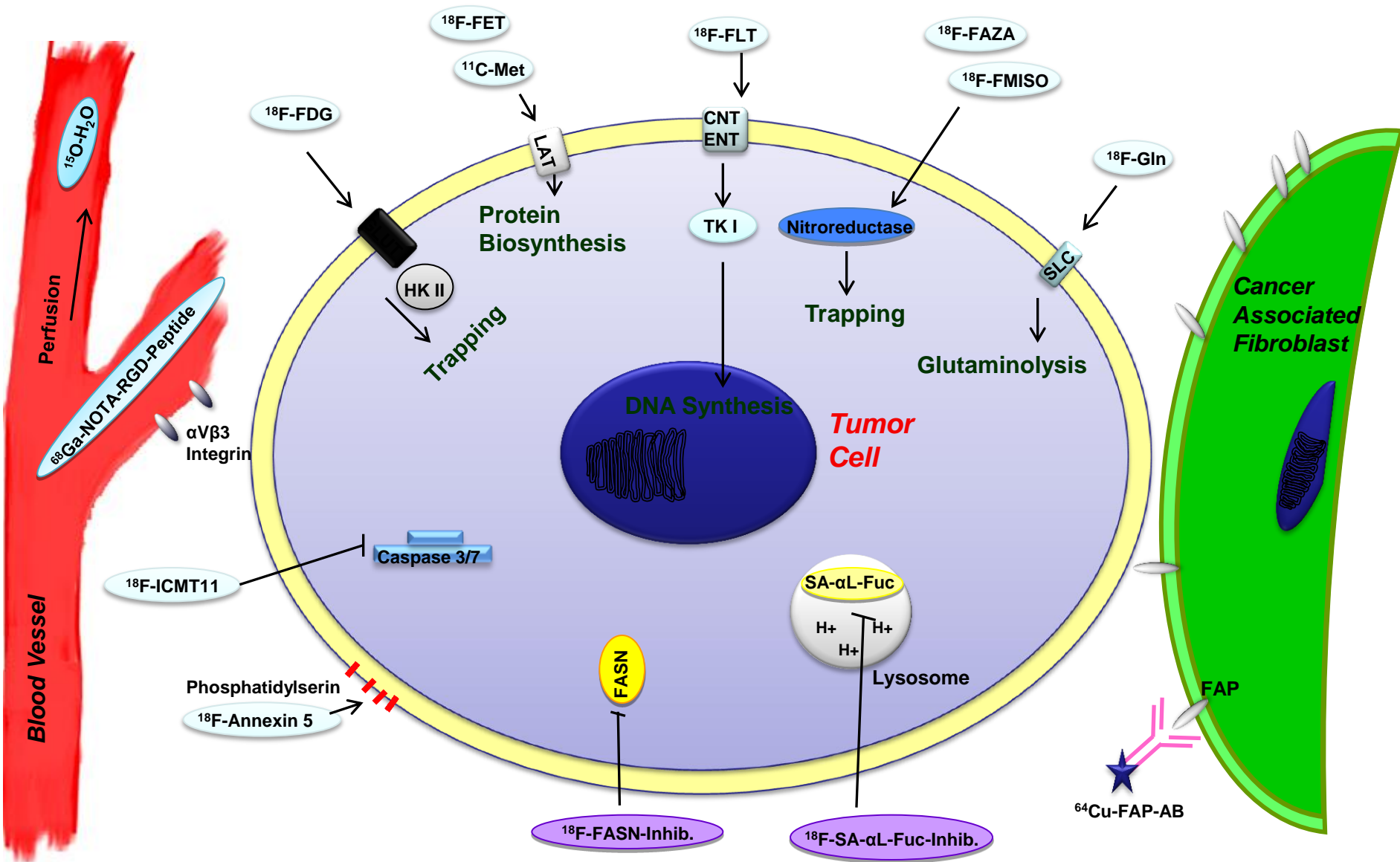
- strong uptake of <sup>64</sup>Cu-DOTA-JF5 in the lungs of *A. fumigatus* infected animals (indicated with the white arrows in Fig. 1)
- quantification of PET/MRI images shows a specific binding of <sup>64</sup>Cu-DOTA-JF5 to *A. fumigatus* infected lung tissue
- the *ex vivo* biodistribution strongly verifies the findings





**Static** PET scans of naïve (left), Gr-1-depleted (middle) and G-CSF stimulated (right) mice 24h after *i.v.* [<sup>64</sup>Cu]DOTA-RB6-8C5 tracer injection. Tracer accumulation was decreased in bones, LNs and spleens of PNM depleted mice and enhanced in G-CSF stimulated mice.

# Molecular Imaging Targets



	Molecular -PET	Morphological-MRI	Functional-MRI	Hyperpolarized Imaging																																												
Non-invasive PET/MR Imaging	<table border="1"> <thead> <tr> <th>Target</th> <th>Biomarker</th> </tr> </thead> <tbody> <tr> <td>Metabolism</td> <td></td> </tr> <tr> <td>• Glucose</td> <td>[<sup>18</sup>F]FDG</td> </tr> <tr> <td>• Aminoacid</td> <td>[<sup>18</sup>F]FET [<sup>11</sup>C]MET [<sup>18</sup>F]GLA</td> </tr> <tr> <td>• Fatty Acid</td> <td>FASN</td> </tr> <tr> <td>Stroma</td> <td>[<sup>64</sup>Cu]FAP</td> </tr> <tr> <td>Proliferation</td> <td>[<sup>18</sup>F]FLT</td> </tr> <tr> <td>Hypoxia</td> <td>[<sup>18</sup>F]FAZA [<sup>18</sup>F]FMISO</td> </tr> <tr> <td>Angiogenesis</td> <td>[<sup>68</sup>Ga]RGD</td> </tr> <tr> <td>Perfusion</td> <td>[<sup>15</sup>O]H<sub>2</sub>O</td> </tr> <tr> <td>Apoptosis</td> <td>[<sup>18</sup>F]ICMT11 [<sup>18</sup>F]Annexin V</td> </tr> <tr> <td>Senescence</td> <td>[<sup>18</sup>F]SA-αL-Fuc</td> </tr> </tbody> </table>	Target	Biomarker	Metabolism		• Glucose	[ <sup>18</sup> F]FDG	• Aminoacid	[ <sup>18</sup> F]FET [ <sup>11</sup> C]MET [ <sup>18</sup> F]GLA	• Fatty Acid	FASN	Stroma	[ <sup>64</sup> Cu]FAP	Proliferation	[ <sup>18</sup> F]FLT	Hypoxia	[ <sup>18</sup> F]FAZA [ <sup>18</sup> F]FMISO	Angiogenesis	[ <sup>68</sup> Ga]RGD	Perfusion	[ <sup>15</sup> O]H <sub>2</sub> O	Apoptosis	[ <sup>18</sup> F]ICMT11 [ <sup>18</sup> F]Annexin V	Senescence	[ <sup>18</sup> F]SA-αL-Fuc	<table border="1"> <thead> <tr> <th>Target</th> <th>Biomarker</th> </tr> </thead> <tbody> <tr> <td>Tissue contrast</td> <td>T<sub>1</sub> T<sub>2</sub> Relaxation • T<sub>1</sub> map • T<sub>2</sub> map GD</td> </tr> </tbody> </table>	Target	Biomarker	Tissue contrast	T <sub>1</sub> T <sub>2</sub> Relaxation • T <sub>1</sub> map • T <sub>2</sub> map GD	<table border="1"> <thead> <tr> <th>Target</th> <th>Biomarker</th> </tr> </thead> <tbody> <tr> <td>Oxygenation</td> <td>BOLD</td> </tr> <tr> <td>Diffusion</td> <td>ADC</td> </tr> <tr> <td>Perfusion</td> <td>BOLD ASL</td> </tr> <tr> <td>Interstitial Pressure</td> <td>XX</td> </tr> <tr> <td>Metabolites</td> <td><sup>1</sup>H Spectroscopy</td> </tr> </tbody> </table>	Target	Biomarker	Oxygenation	BOLD	Diffusion	ADC	Perfusion	BOLD ASL	Interstitial Pressure	XX	Metabolites	<sup>1</sup> H Spectroscopy	<table border="1"> <thead> <tr> <th>Target</th> <th>Biomarker</th> </tr> </thead> <tbody> <tr> <td>Enzyme Activity</td> <td>Lactate Pyruvate</td> </tr> </tbody> </table>	Target	Biomarker	Enzyme Activity	Lactate Pyruvate
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Morphological-MRI

Functional-MRI

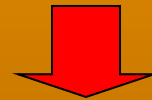
Hyperpolarized  
Imaging

Non-invasive PET/MR Imaging

**Metabolomics**

**Proteomics**

**Data Mining**



**Clinical Relevance**