

# Theranostic R&D in CERIMED : European Medical Imaging Research Center



CERIMED

Montpellier

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CERIMED UMS 2012 AMU CNRS  
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Radiopharmacy APHM



Marseille  
Center for CardioVascular  
and Nutrition research



# *Our research in Theranostic*

3 main Axes

## 1) Innovative vascular molecular targets for Imaging and theragnostic approaches

Angiomotin

APJ

## 2) R&D in vectorisation and radiolabelling

Nanosystem, nanobodies as carrier

BBB disruption

Microfluidic for radiolabelling

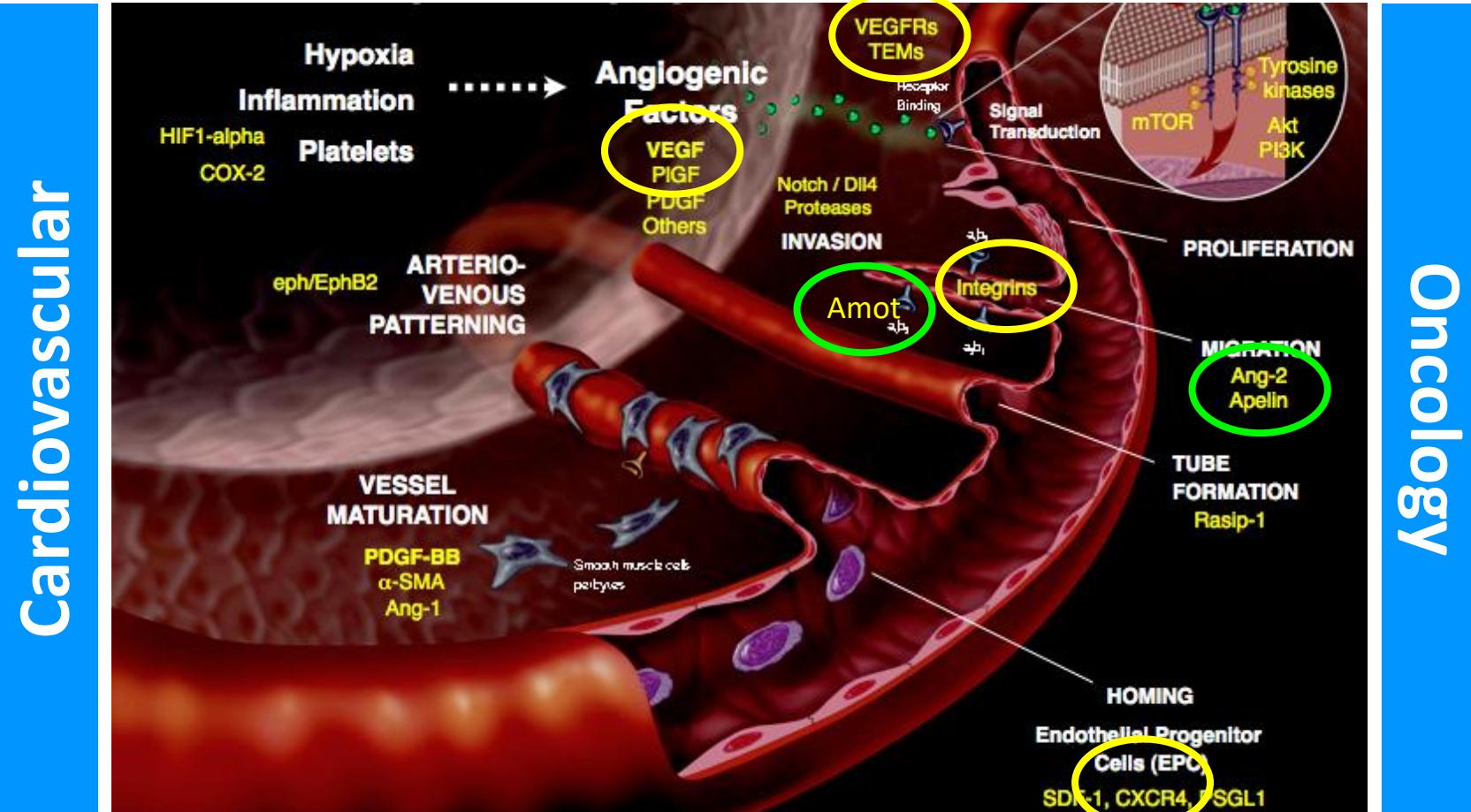
## 3) Optimization of already validated VIR

PSMA and salivary glands

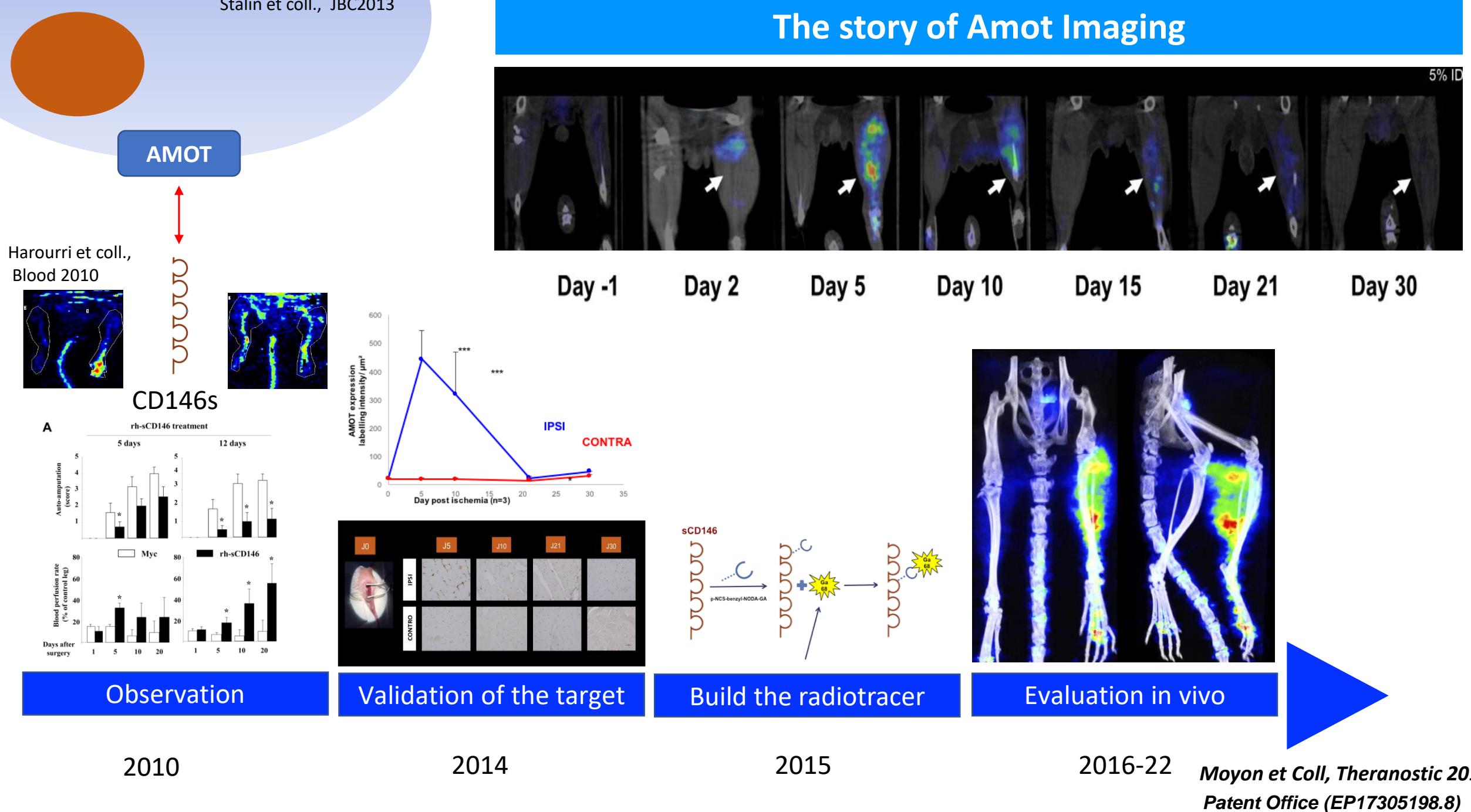
Predictive tools of toxicity

# *Our research in Theranostic*

## 1) Innovative vascular molecular targets for Imaging and theragnostic approaches

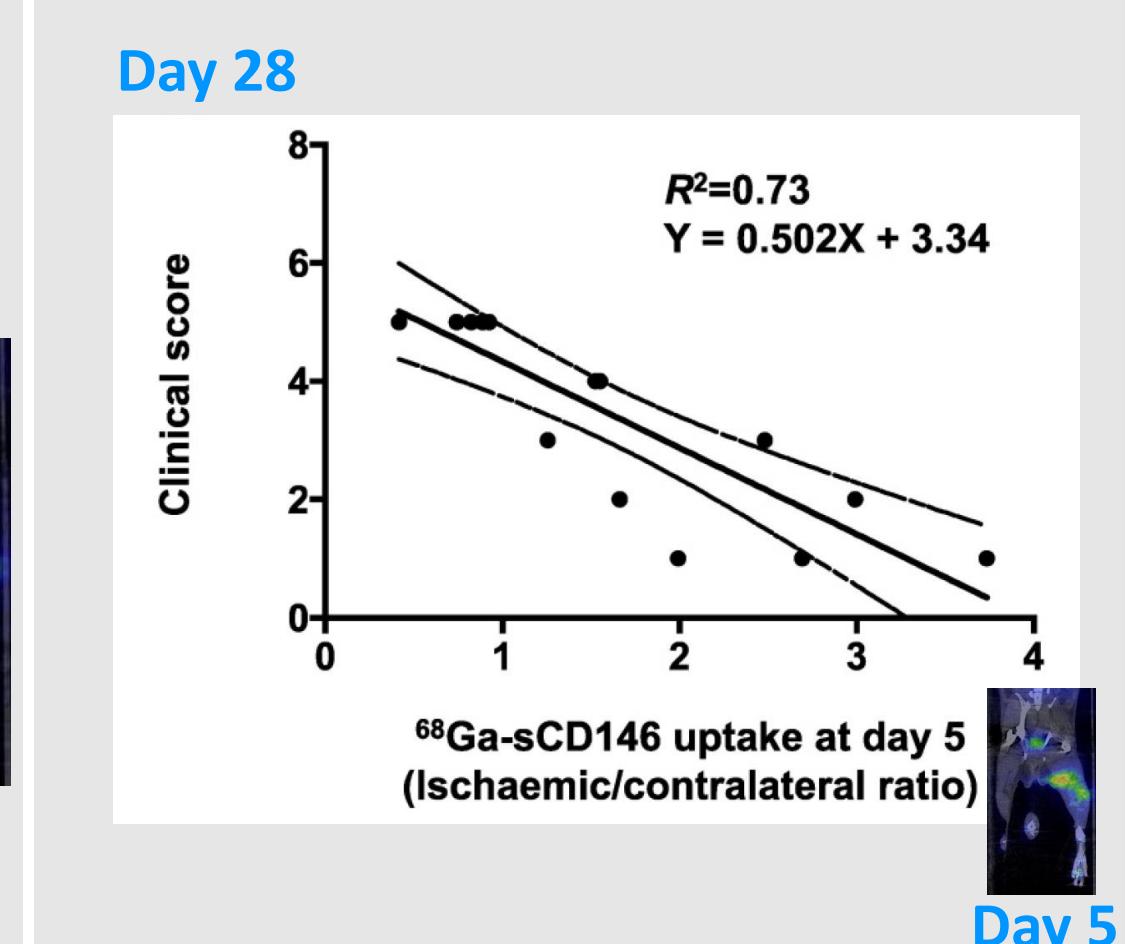
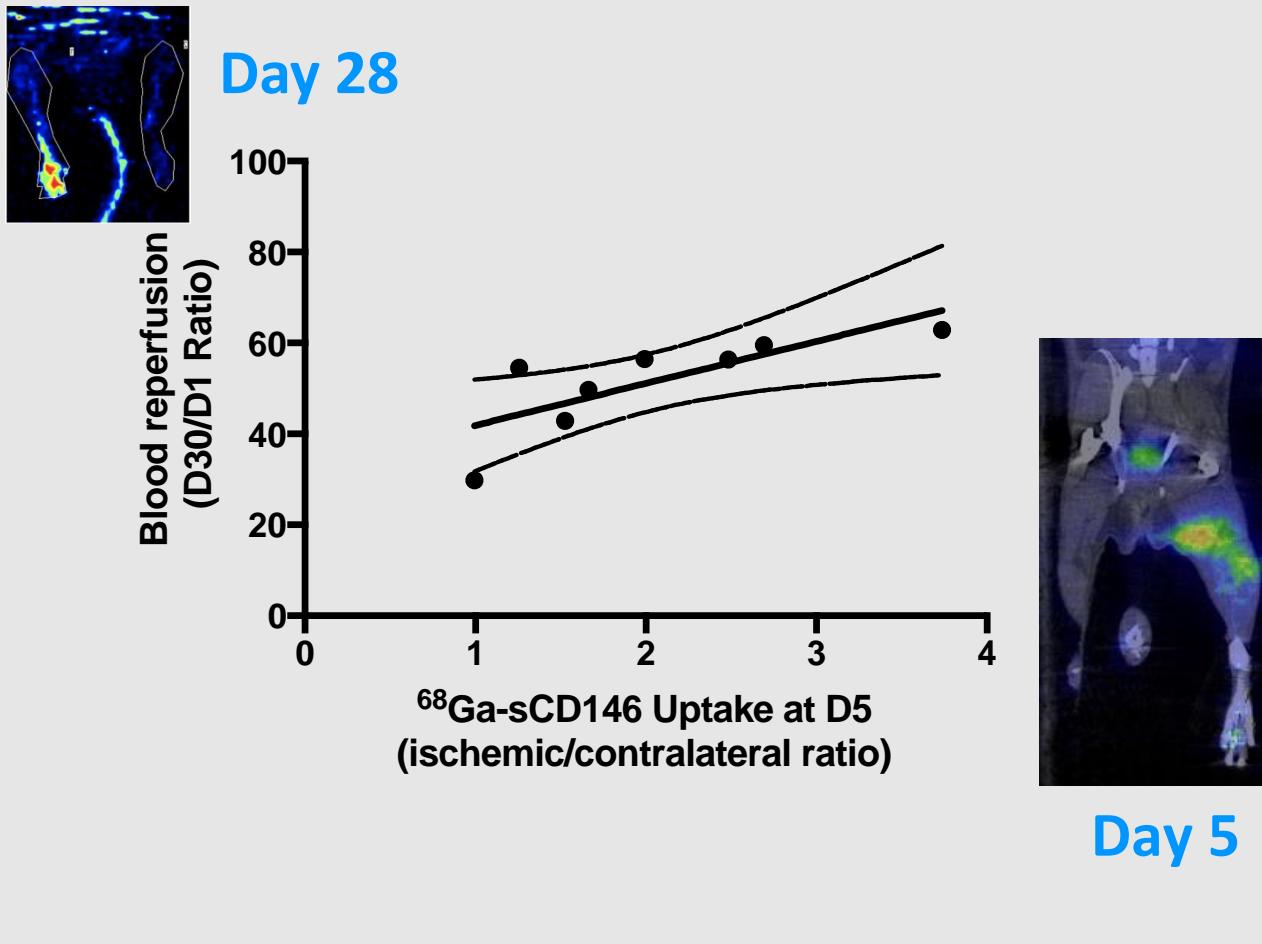


# The story of Amot Imaging



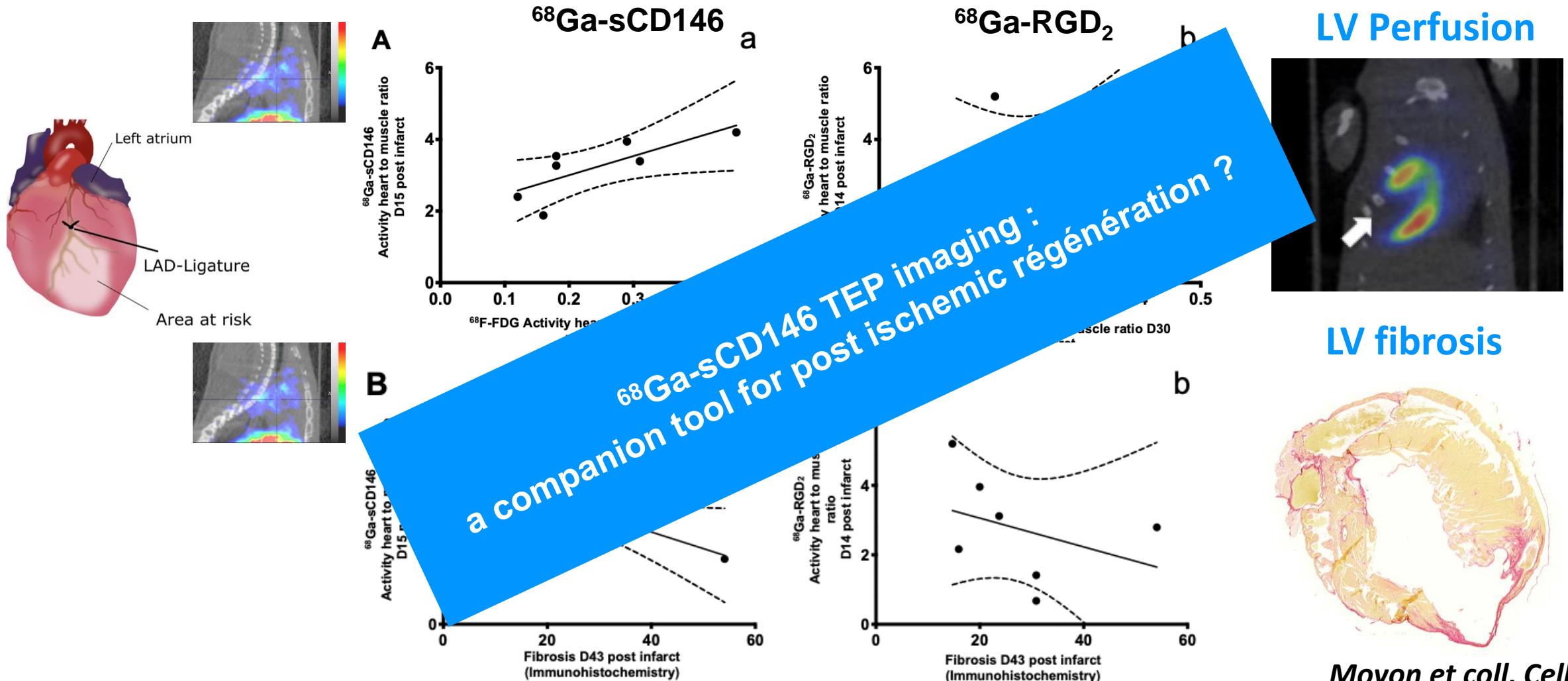
# $^{68}\text{Ga}$ -sCD146 TEP imaging predicts post ischemic rescue

$^{68}\text{Ga}$ -sCD146 early predictive tool of hindlimb recovery

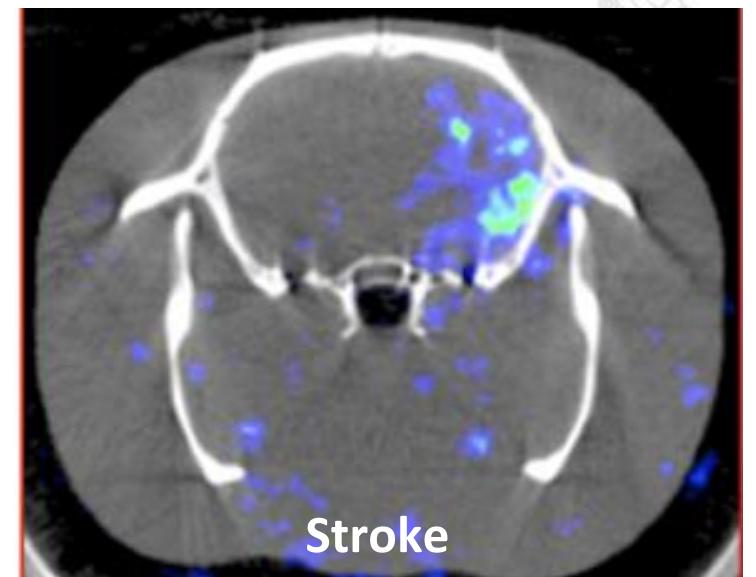
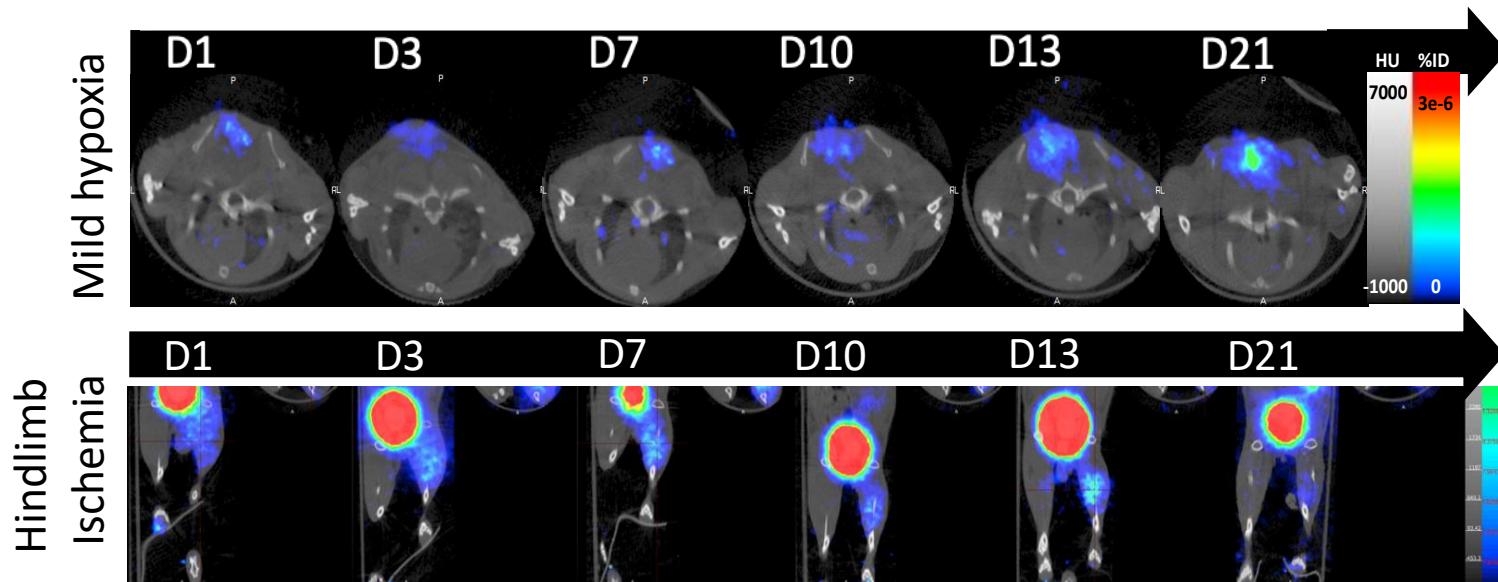
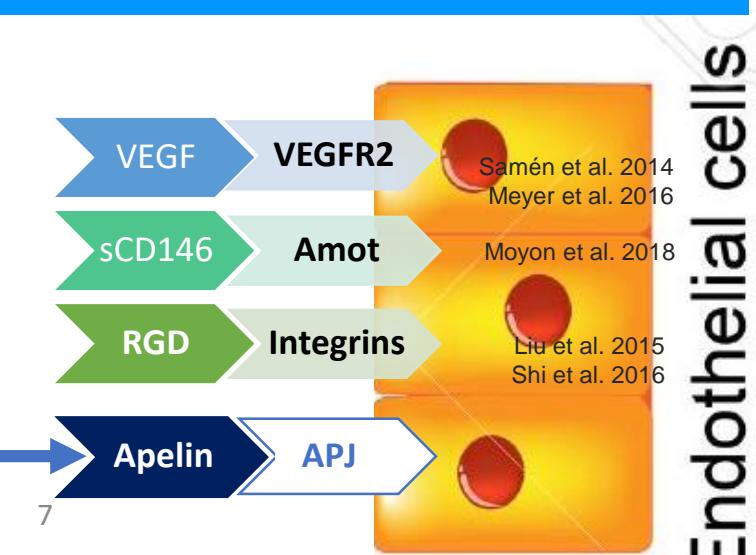
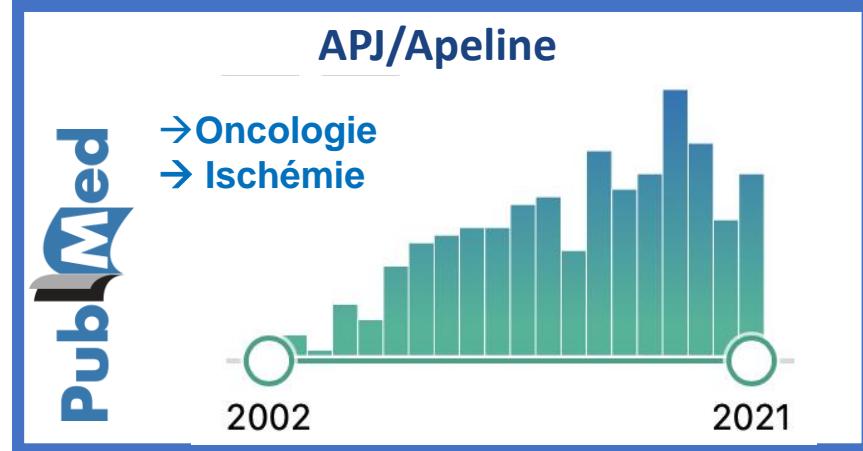
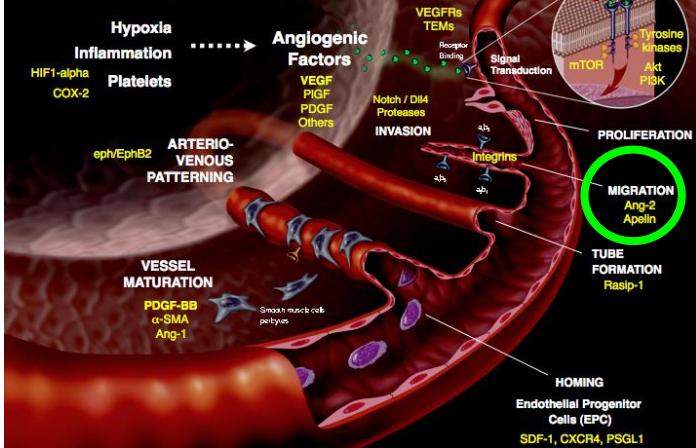


# $^{68}\text{Ga}$ -sCD146 TEP imaging predicts post ischemic rescue

## Myocardial infarction



# Apelin/APJ for TEP imaging of angiogenesis



# Are vascular targets may help for tumor targeting ?

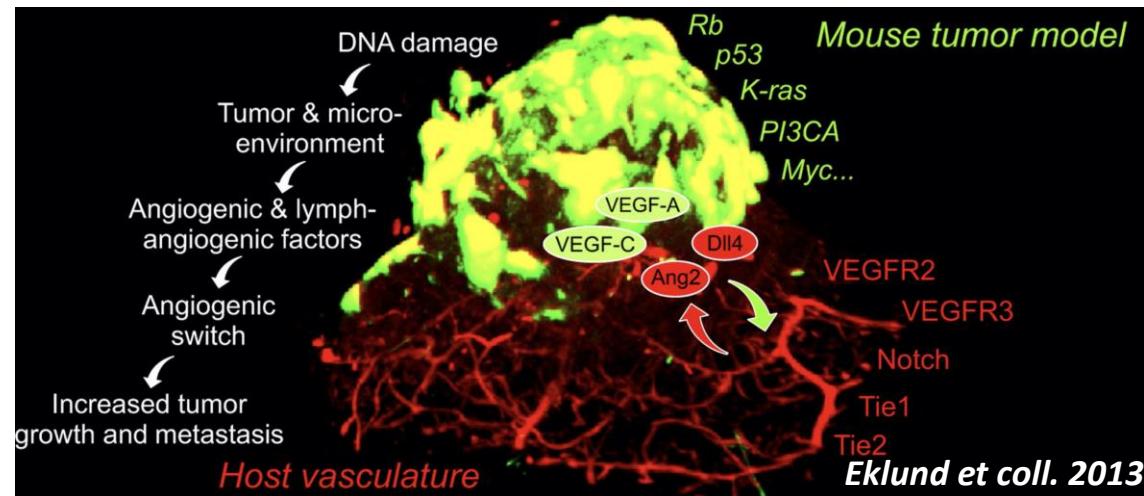
## Tumor Angiogenesis: Therapeutic Implications

Judah Folkman, M.D.



The NEW ENGLAND  
JOURNAL of MEDICINE

1971



## *Tumor expression of activated endothelial biomarkers*

Amot Family	Cancer Types	Function	Possible Mechanism	Ref.
Amot	Breast cancer	Oncogene	Increasing the expression of YAP, TAZ and LATS1 and enhancing ERK1/2 pathway	[19,38-40]
	Osteosarcoma	Oncogene	Unknown	[44,45]
Amot-p80	Prostate cancer	Oncogene	Unknown	[46]
	HNSCC	Oncogene	Unknown	[47]
Amot-p130	Hepatic carcinoma	Oncogene	Augmenting the activity of YAP	[5]
	Renal cell cancer	Oncogene	Increasing the YAP-related TEAD promoter activity.	[6]
Amotl1	Ovarian cancer	Tumor suppressor	Inhibiting the activation of YAP target genes	[50]
	Lung cancer	Tumor suppressor	Sequestering oncogenic YAP/TAZ and decreasing Cyr61 expression	[51]
	Breast cancer	Oncogene	Stimulating Src activity	[41]
Amotl2	Cervical cancer	Oncogene	Unknown	[48]
	Colon cancer	Oncogene	Disrupting the apical-basal polarity.	[27]
Glioblastoma	Tumor suppressor	Inhibiting the activation of YAP target genes		[49]

Apelin and APJ expression in various cancer tissues/serum and cell lines.

Cancer type	Tumor tissue/serum		Cell lines	
	mRNA	Protein	mRNA	Protein
Gastroesophageal			Apelin	
Endometrium			Apelin	
Ovarian		Apelin/APJ	Apelin/APJ	Apelin/APJ
Cervical		Apelin		
Lung	Apelin/APJ	Apelin/APJ	Apelin	Apelin
Colon	Apelin/APJ	Apelin/APJ	Apelin/APJ	Apelin/APJ
Multiple myeloma		Apelin		
OSCC		Apelin	Apelin	Apelin
Pancreas	Apelin	Apelin/APJ		
Gastric		Apelin/APJ		
Breast		Apelin	Apelin	Apelin/APJ
Brain	Apelin/APJ	Apelin/APJ	Apelin	
RCC	Apelin			
HCC	Apelin		Apelin/APJ	
CCA	Apelin/APJ		APJ	
Prostate	Apelin			
Skin	Apelin			Apelin/APJ

Abbreviations: APJ - apelin receptor; OSCC - oral squamous cell carcinoma; RCC - renal cell carcinoma; HCC - hepatocellular carcinoma; CCA - cholangiocarcinoma

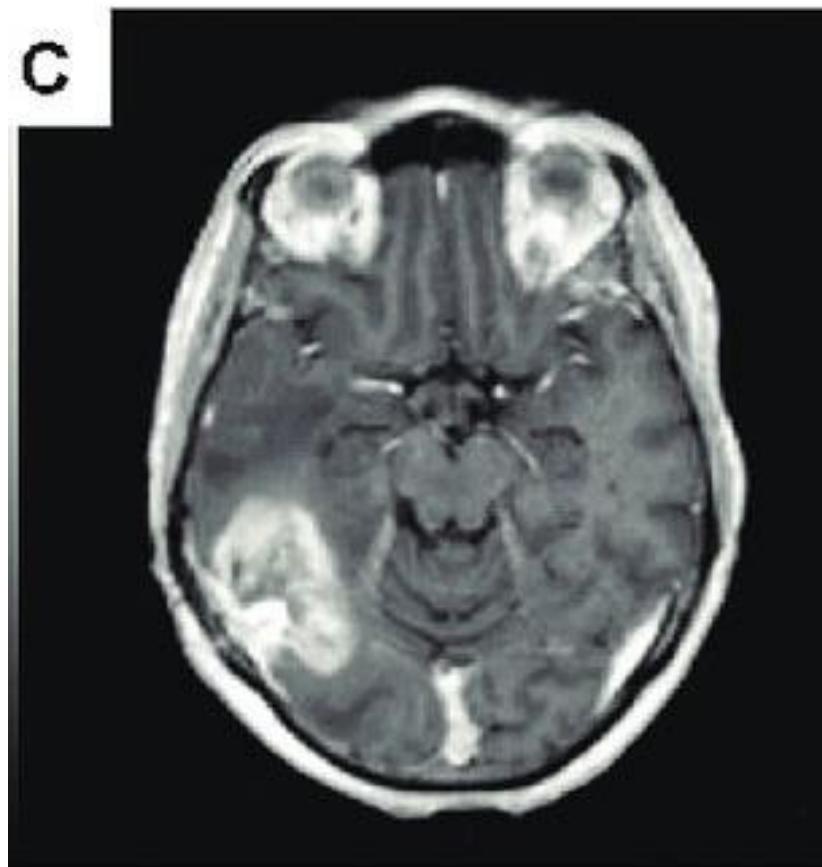
AMOT

APJ

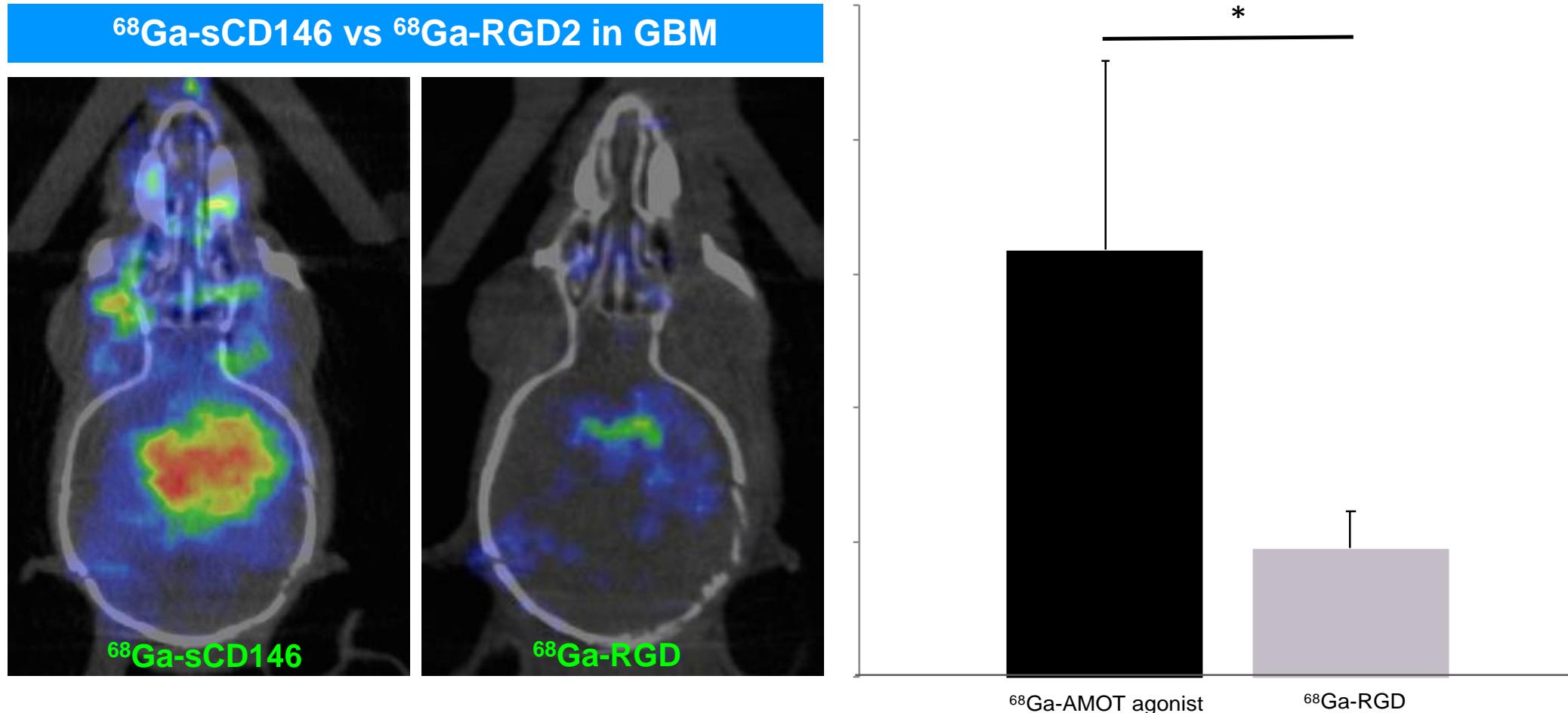
Massoumi et coll. 2020

# Already the case for integrin

MRI T1w + Gd-DTPA

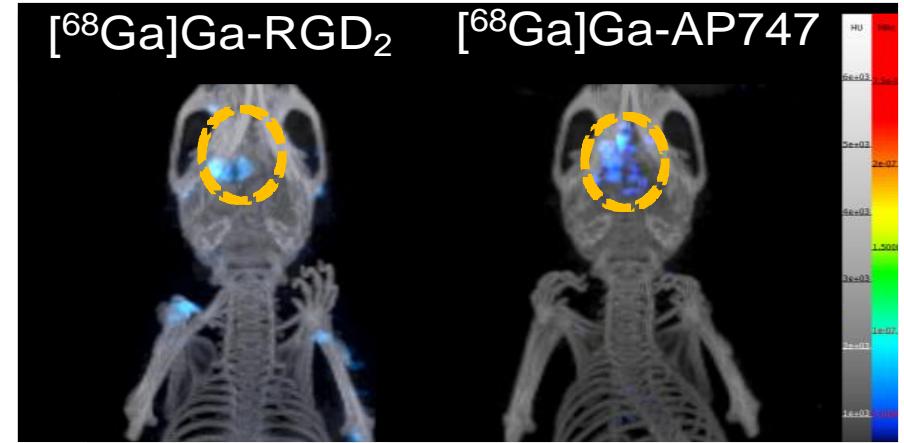
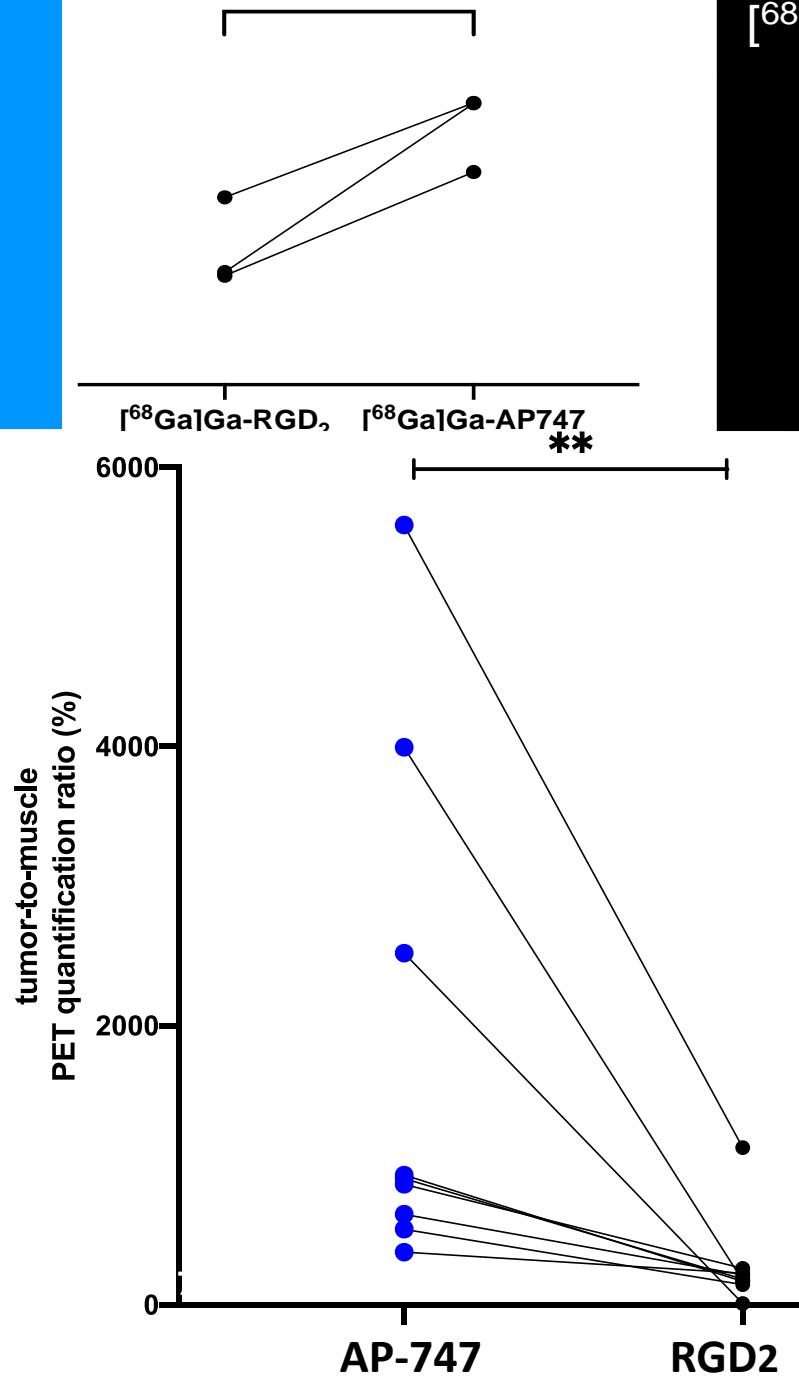
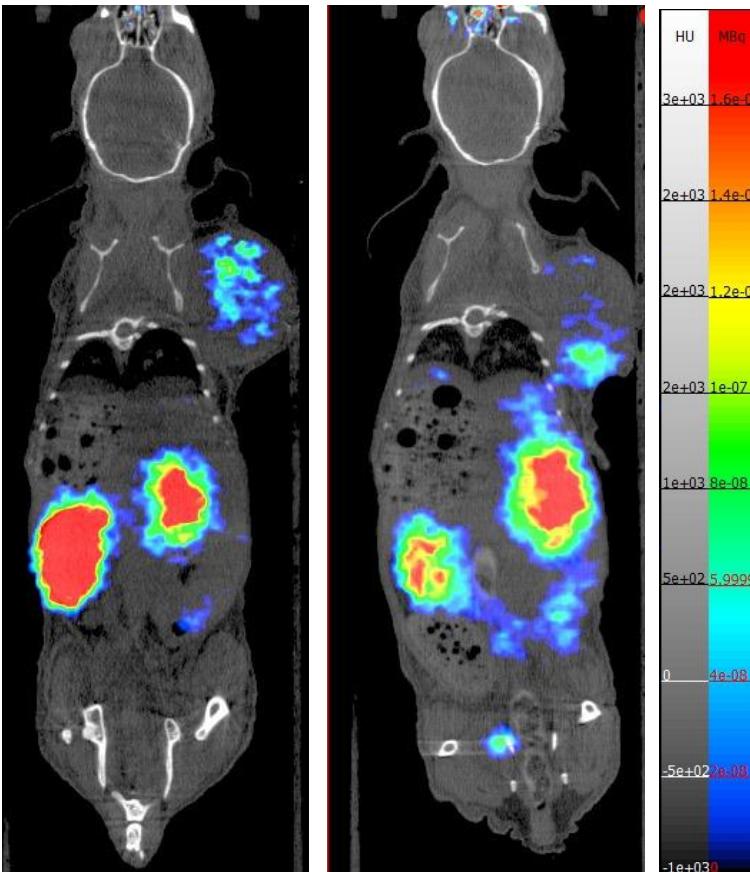


# AMOT : $^{68}\text{Ga}$ -sCD146 imaging in Glioblastoma



# APJ

## $^{68}\text{Ga}$ -AP747 imaging in Glioblastoma



APJ

## $^{68}\text{Ga}$ -AP747 imaging in Colon ADK

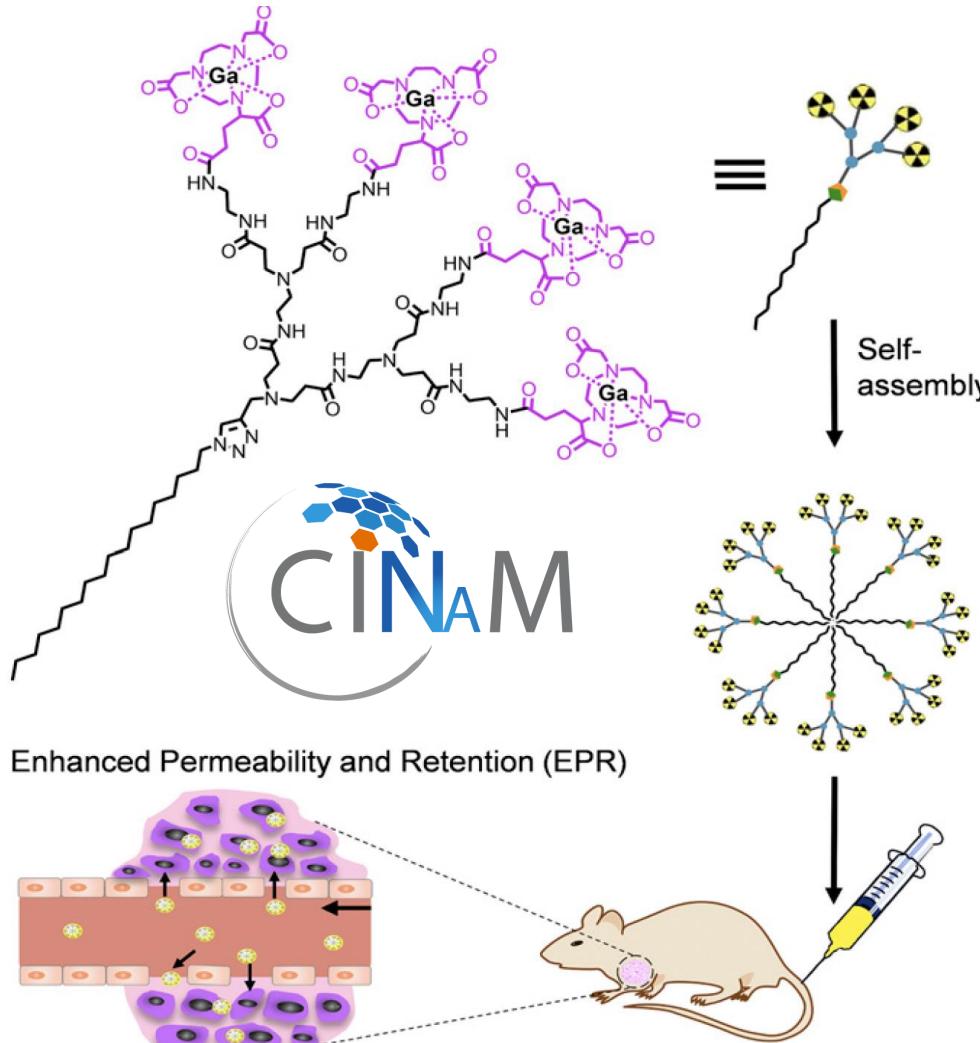
$\downarrow$

$^{177}\text{Lu}$  radiolabeling

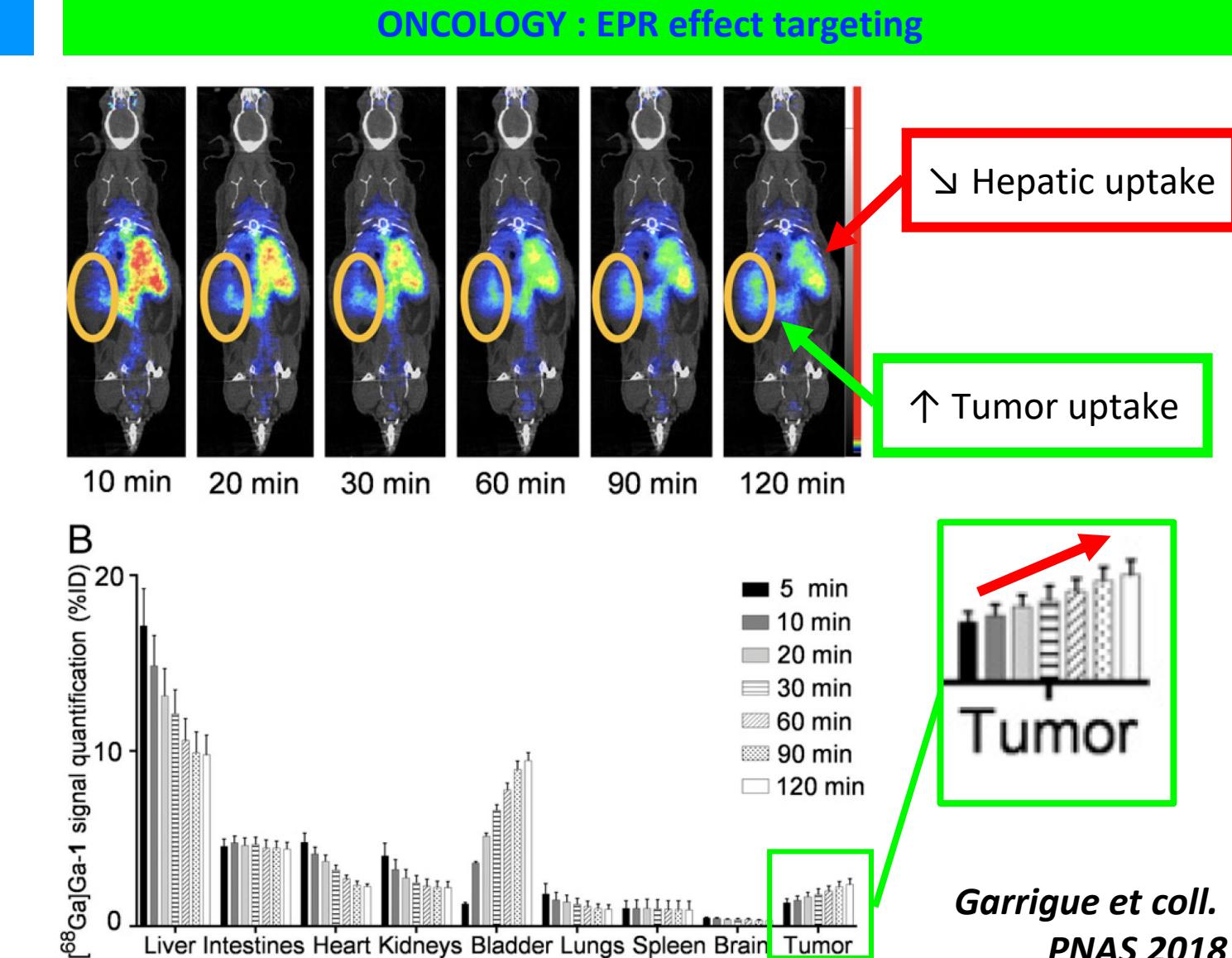
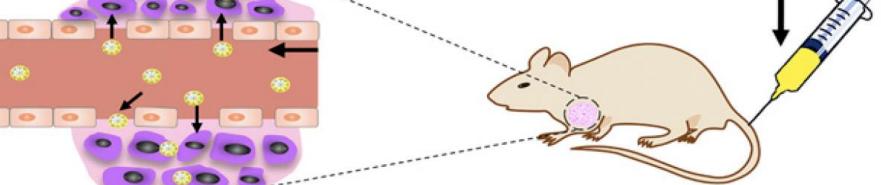
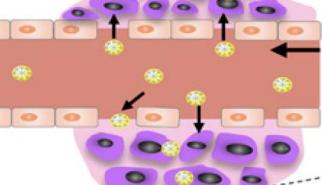
EP 20 305665 , PCT/EP2021/066707

# *Our research in Theranostic*

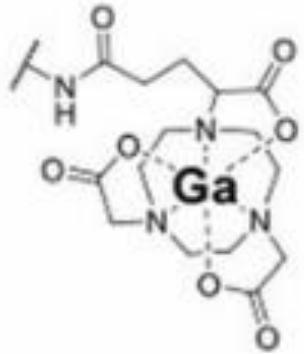
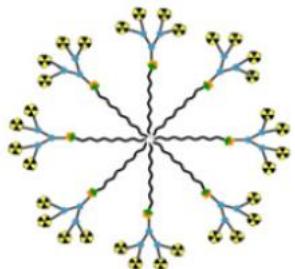
## 2) R&D in vectorisation and radiolabeling



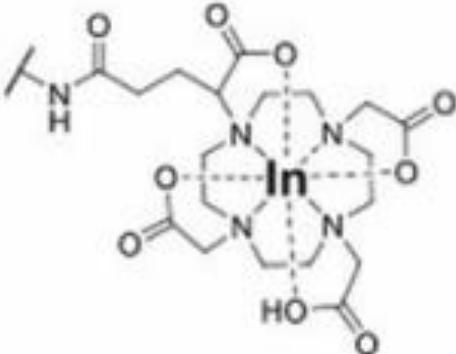
Enhanced Permeability and Retention (EPR)



# A self-assembling amphiphilic dendrimer nanotracer for SPECT imaging†

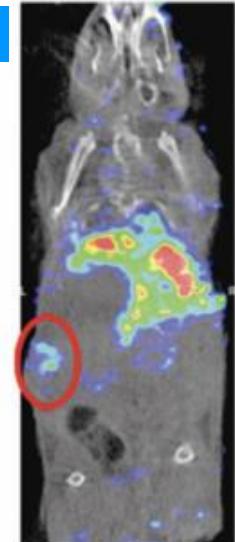
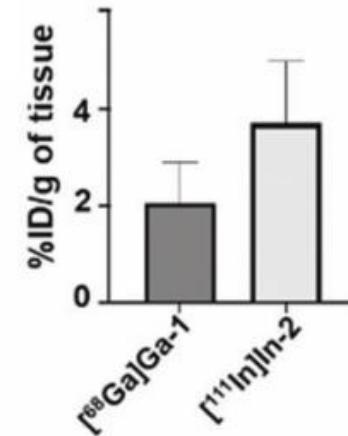
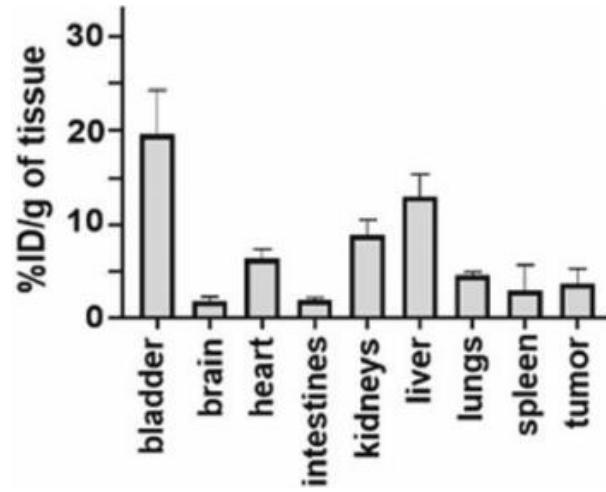


**Ga-1**



**In-2**

Biodistribution of  $[111\text{In}]\text{In-2}$  quantified by  $\mu\text{SPECT/CT}$  180 min p.i.

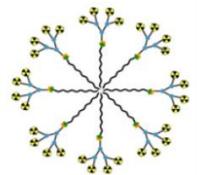


Tumor uptake of  $[111\text{In}]\text{In-2} \rightarrow$

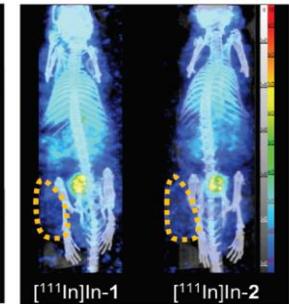
Almost 2-fold higher than that of  $[68\text{Ga}]$  Ga-1

BUT also hepatic uptake of  $[111\text{In}]\text{In-2}$  was 2-fold higher

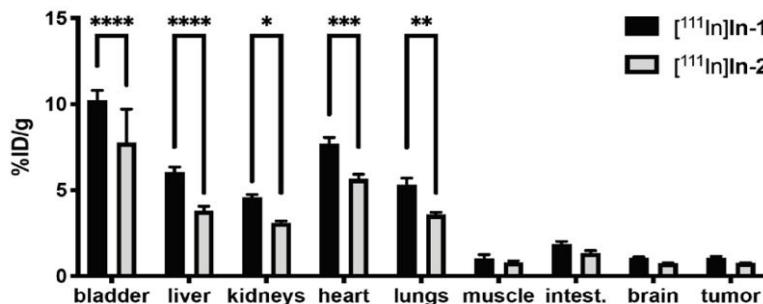
# Optimization of dendrimers PK for isotopic imaging : DOTA vs. NOTA ?



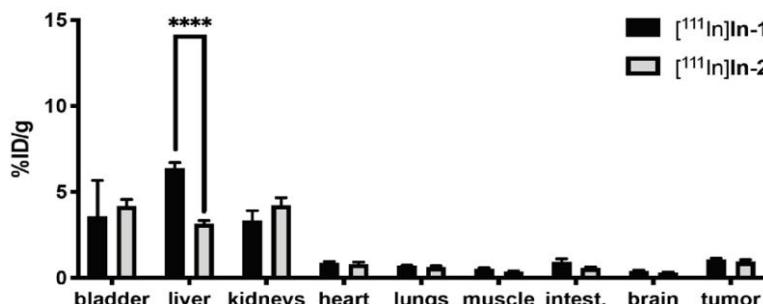
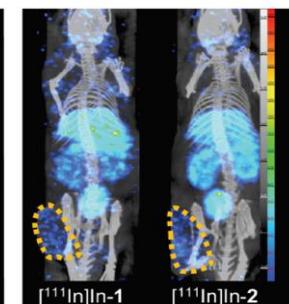
2h p.i.



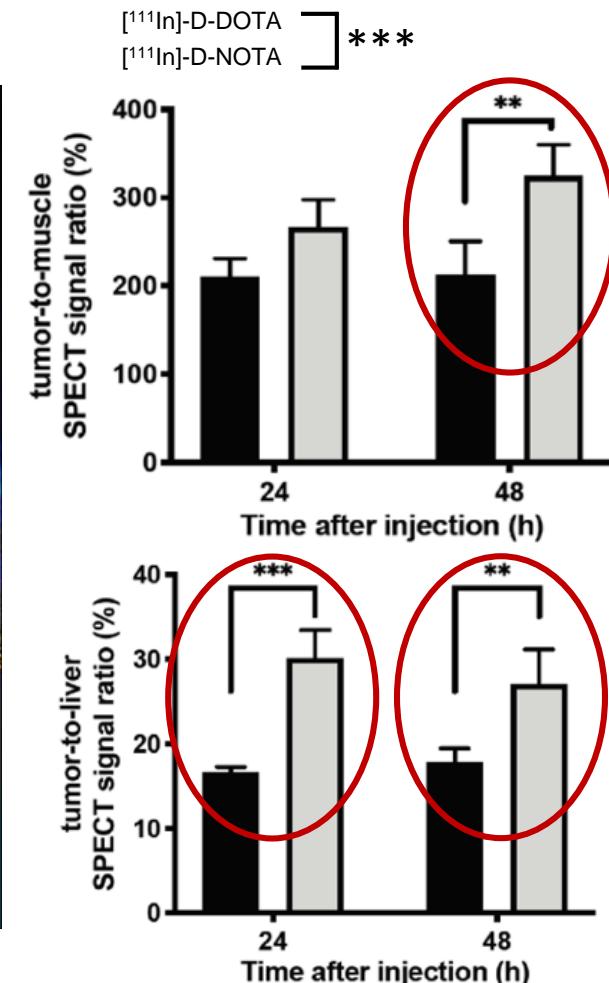
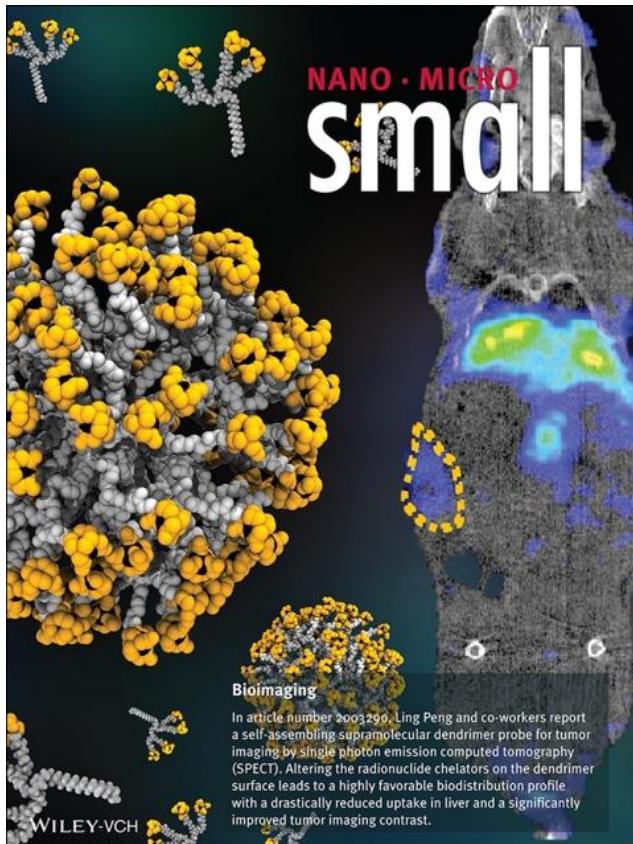
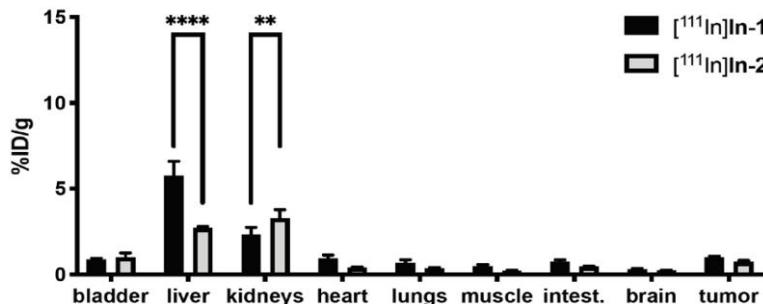
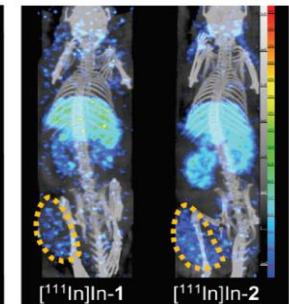
$[^{111}\text{In}]In\text{-}1$  :  $[^{111}\text{In}]\text{-C}_{18}\text{-G}_2\text{-DOTA}$   
 $[^{111}\text{In}]In\text{-}2$  :  $[^{111}\text{In}]\text{-C}_{18}\text{-G}_2\text{-NOTA}$



24h p.i.

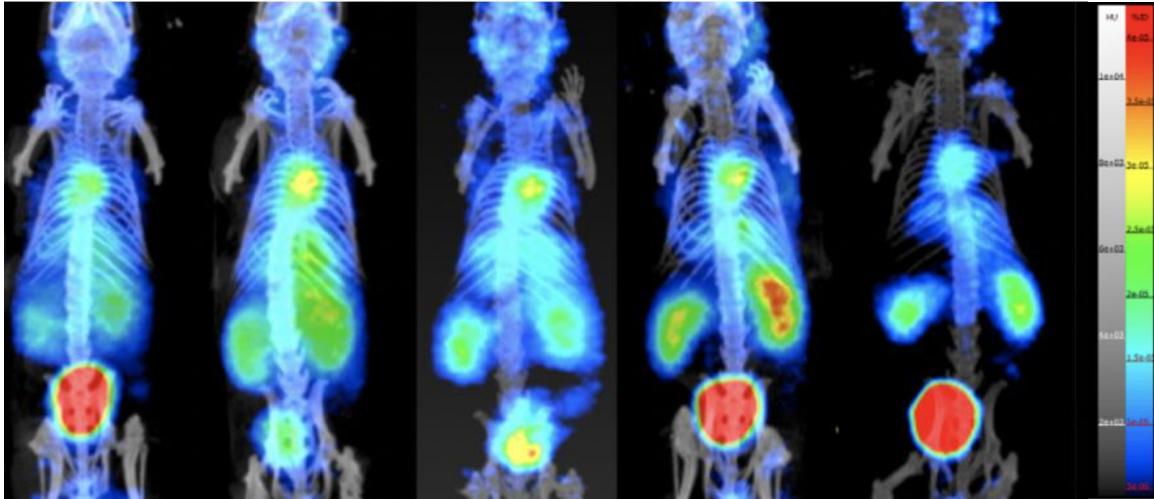


48h p.i.

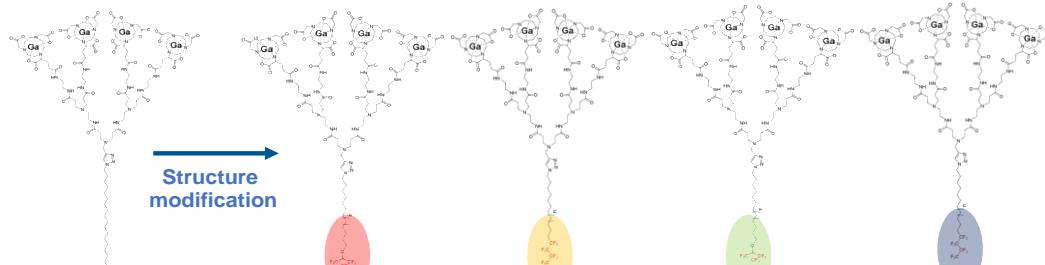


**NOTA → Tumor/Tissue ratio**

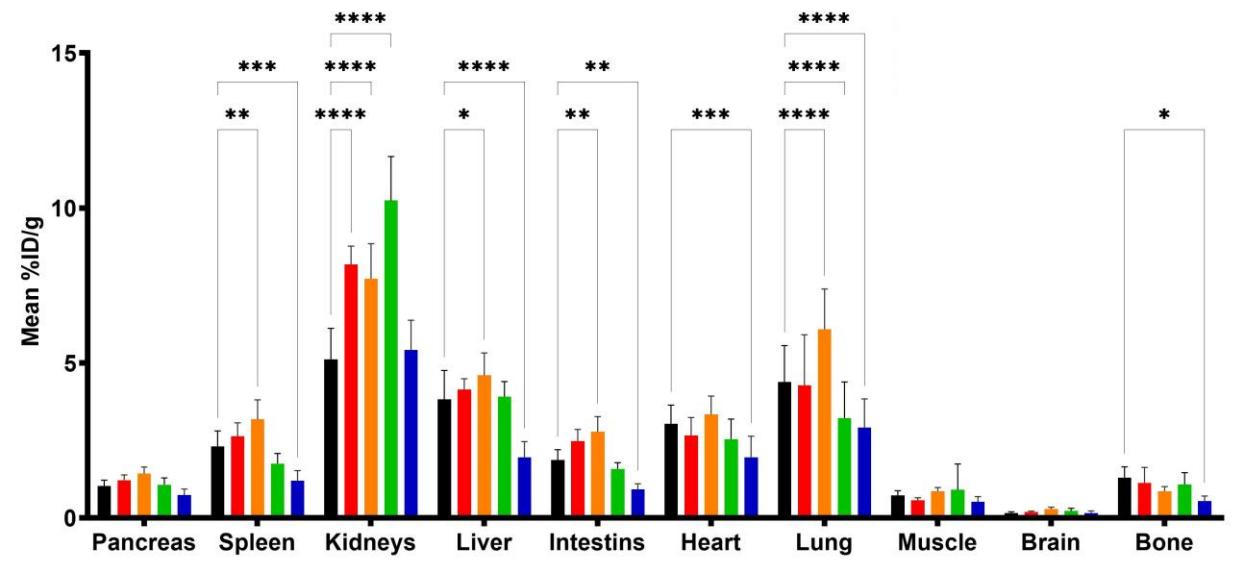
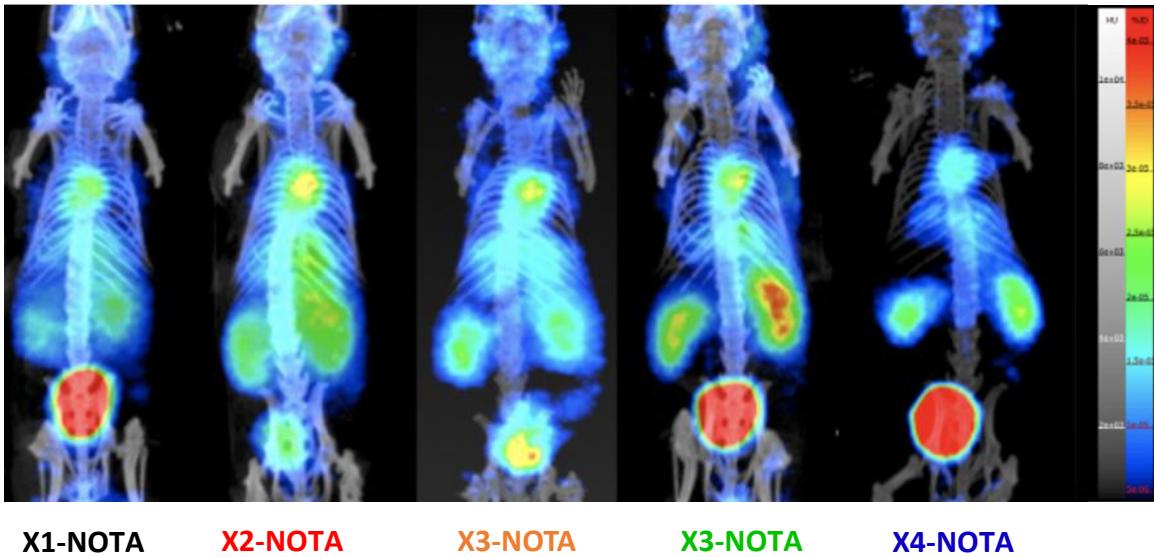
# Optimization of dendrimers PK for isotopic imaging : New chemical modulations



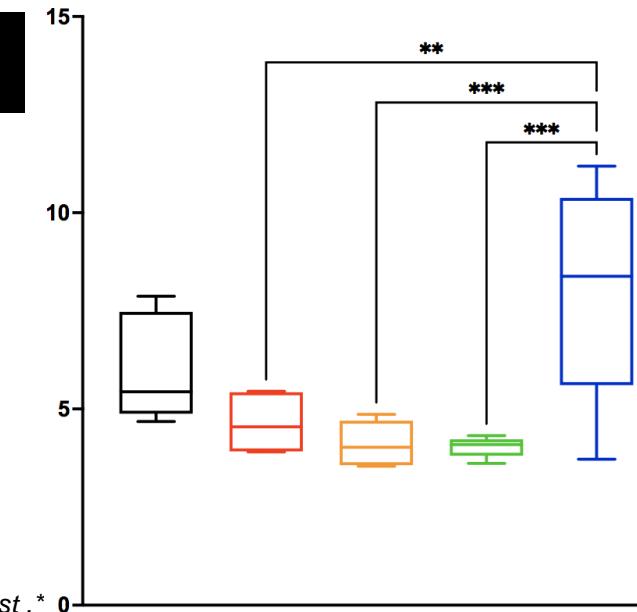
X1-NOTA    X2-NOTA    X3-NOTA    X3-NOTA    X4-NOTA



# Optimization of dendrimers PK for isotopic imaging : New chemical modulations



Plasmatic volume of distribution (mL)

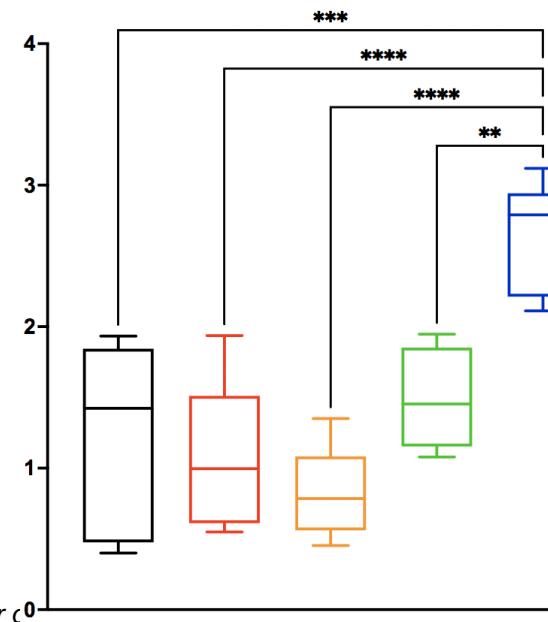


COMPO

COMputational  
Pharmacology  
and clinical Oncology

Two-way ANOVA post-hoc Dunnet's test , \* 0

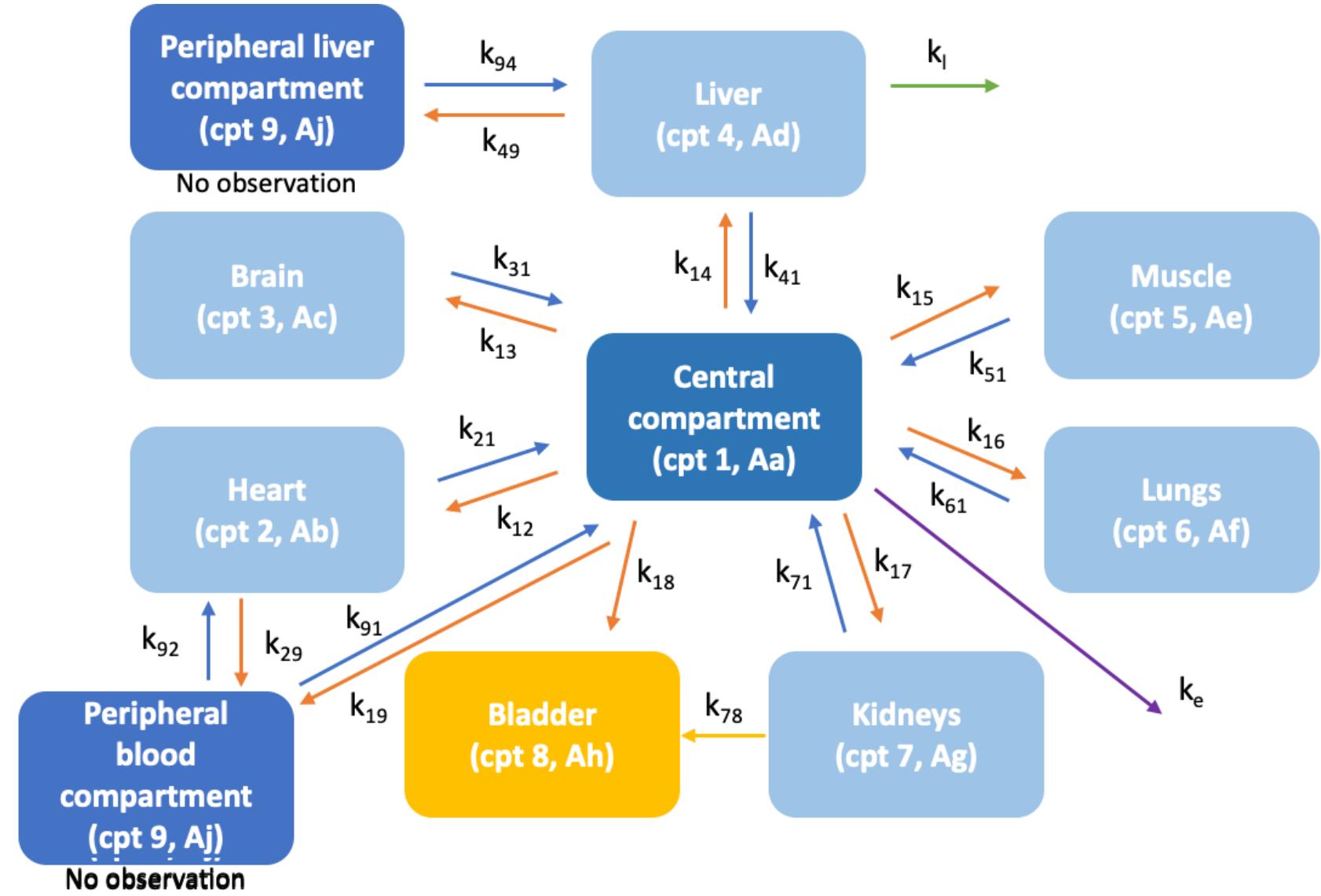
Plasmatic clearance (mL/h)



# Optimization of dendrimers PK for isotopic imaging : PK Modeling

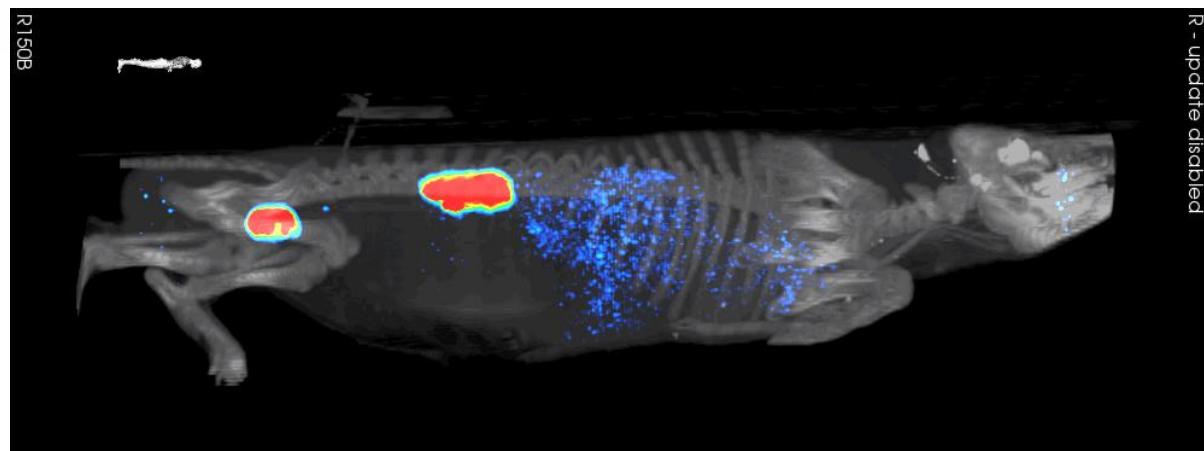
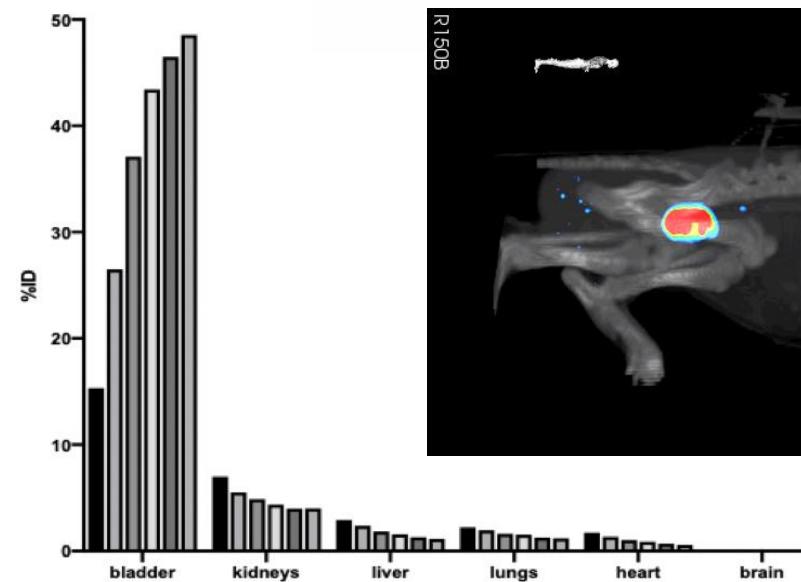
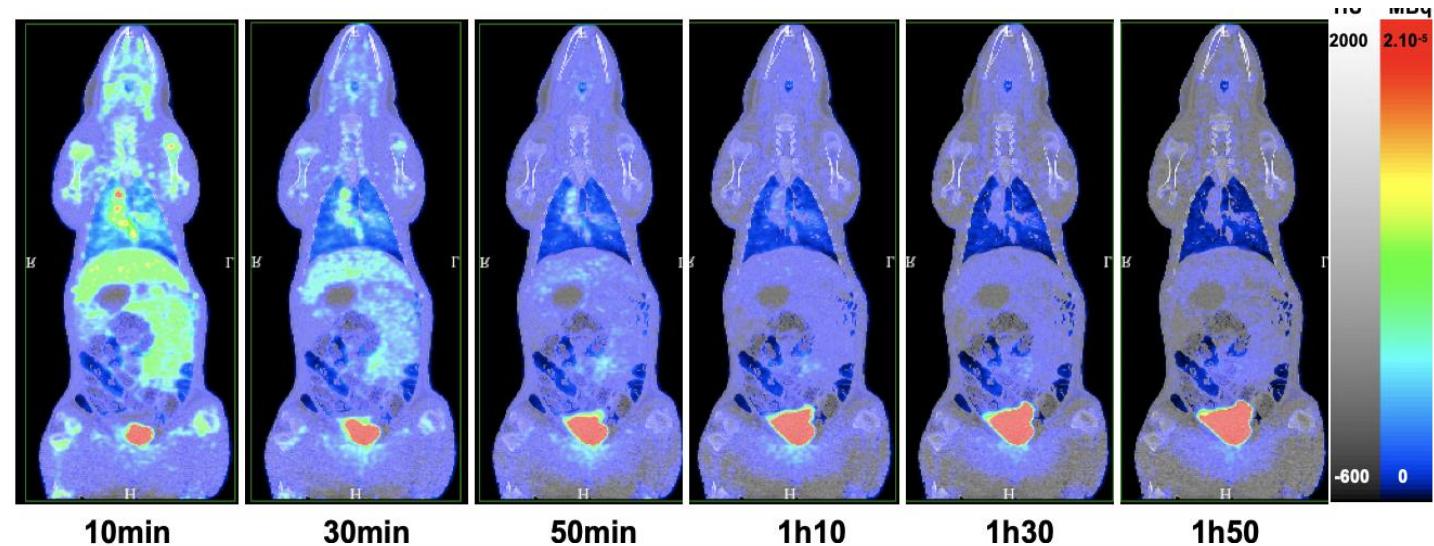
**COMPO**

COMputational  
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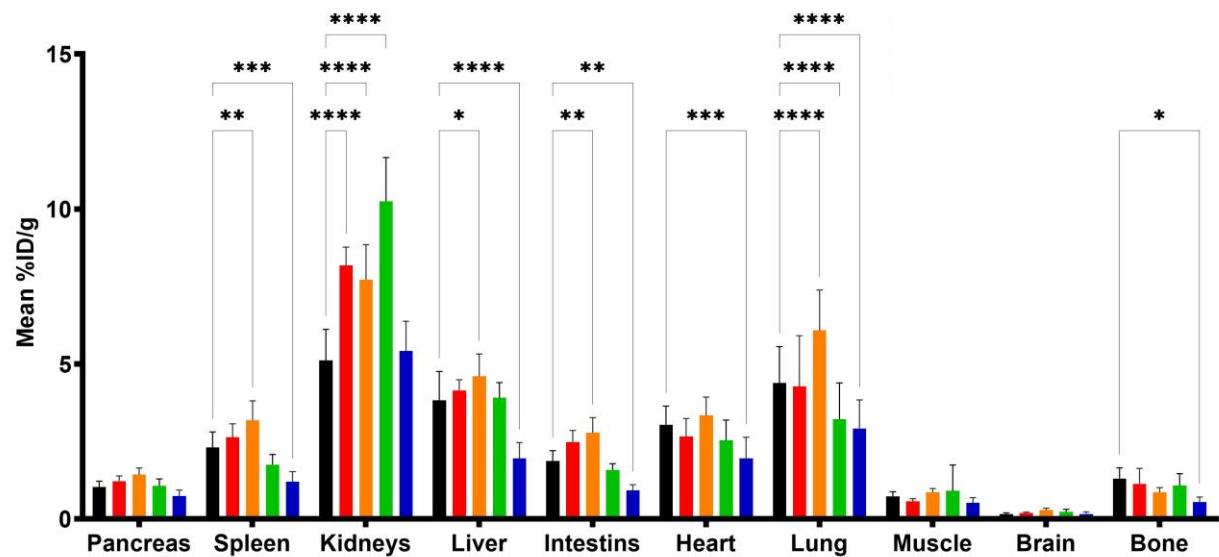
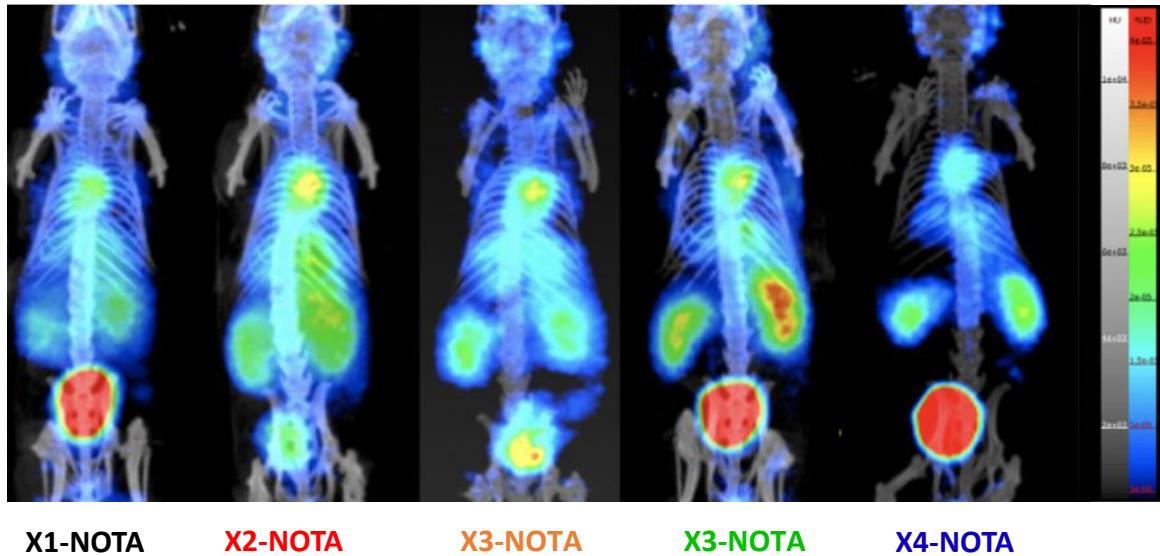


# *Our research in Theranostic*

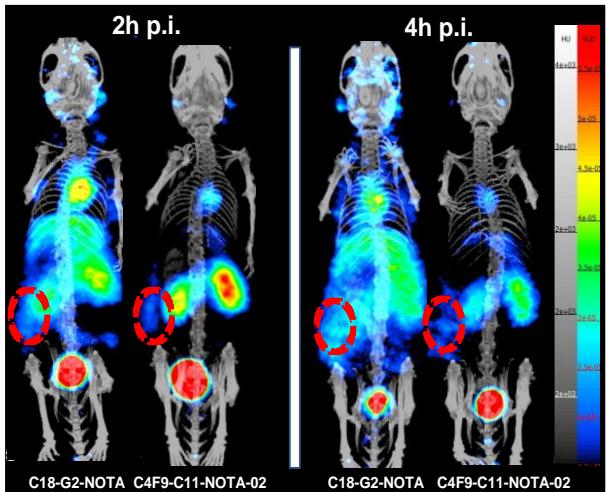
## Pharmacokinetics in large animal SWINE/MONKEYS



# Optimization of dendrimers PK for isotopic imaging : new chemical modulations

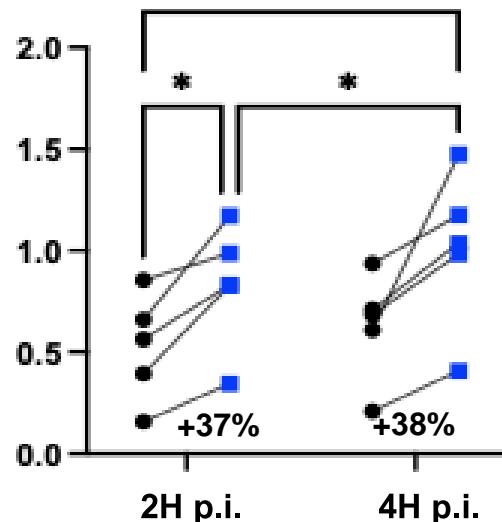


## Pancreatic adenocarcinoma

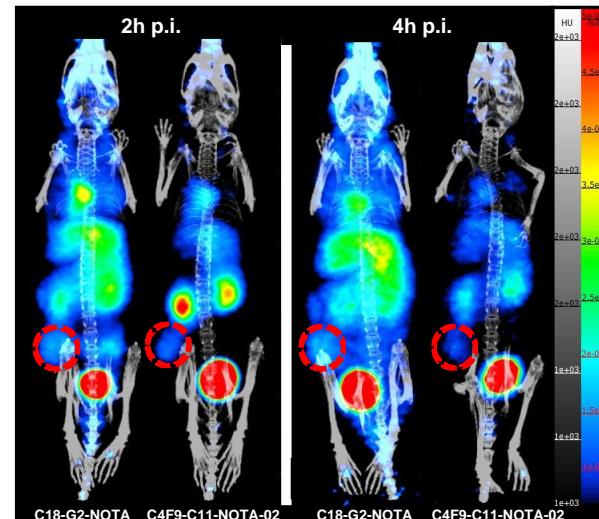


X1-NOTA

X4-NOTA

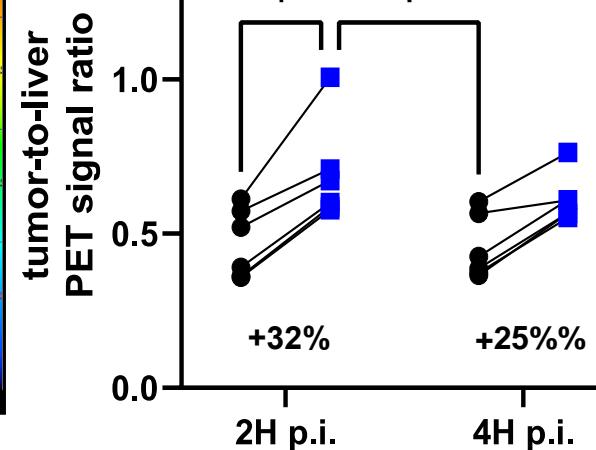


## Ectopic glioblastoma

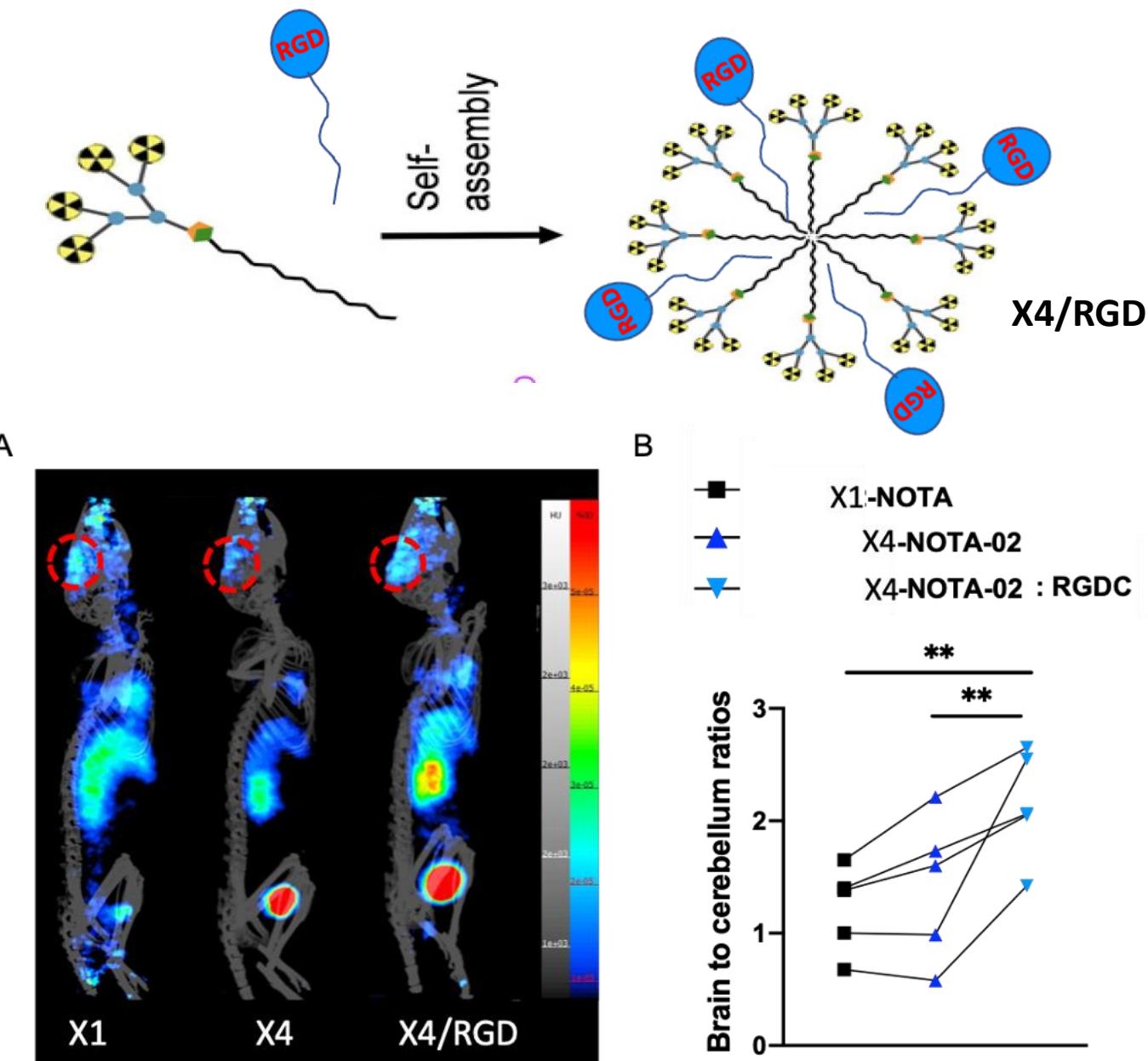


X1-NOTA

X4-NOTA



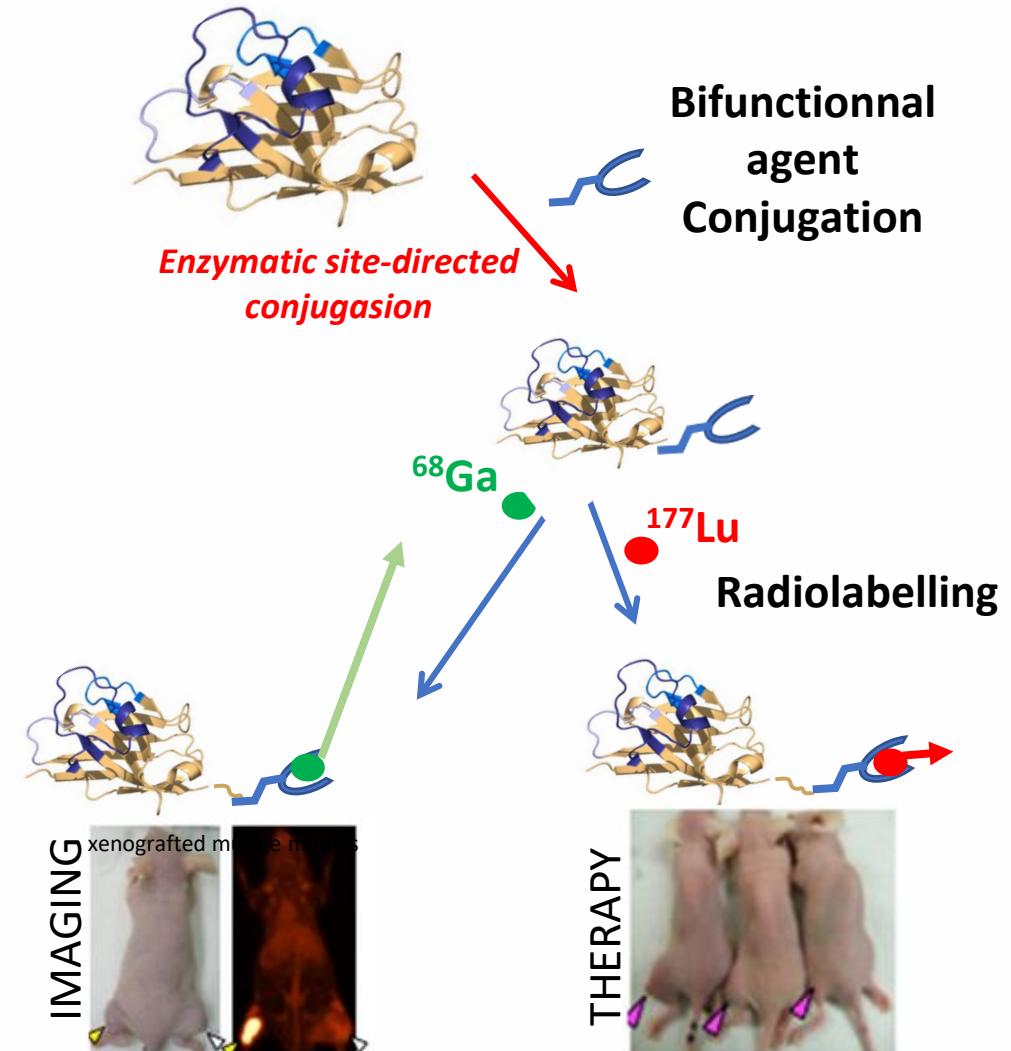
# Optimization of dendrimers PK for isotopic imaging : targeting



# *Our research in Theranostic*

## *Other Tumor targeting strategies*

### Radiolabelled nanobodies production line

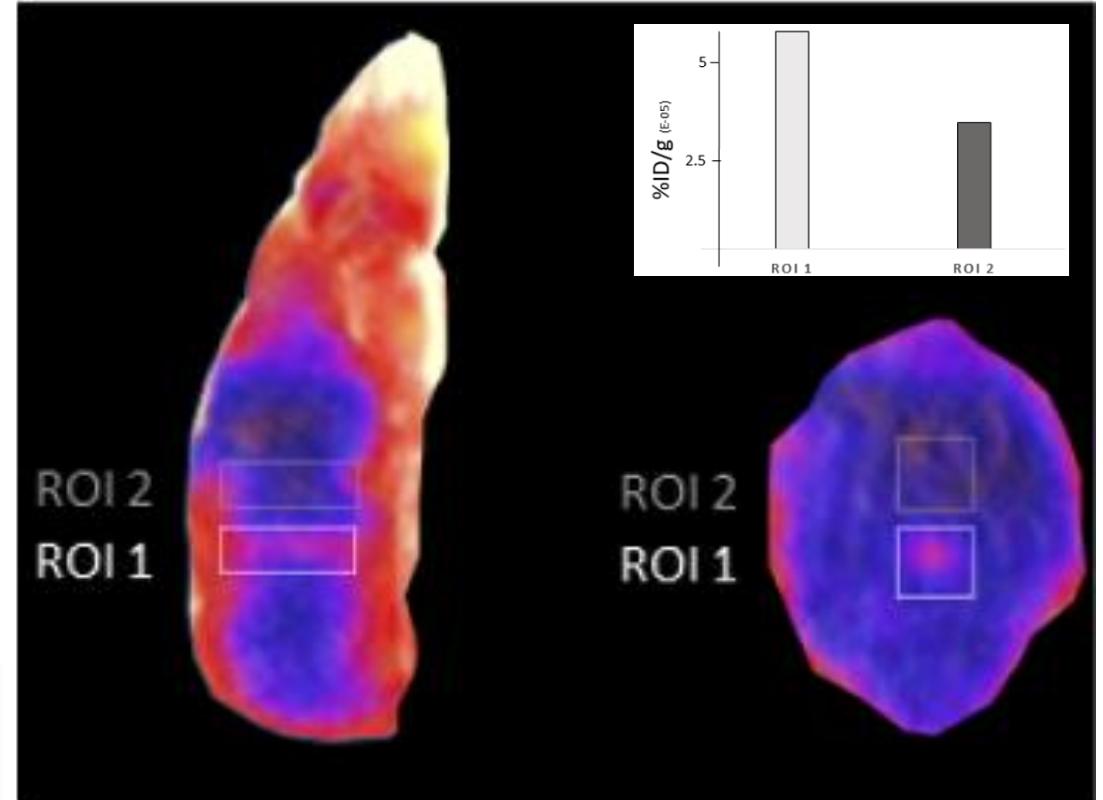
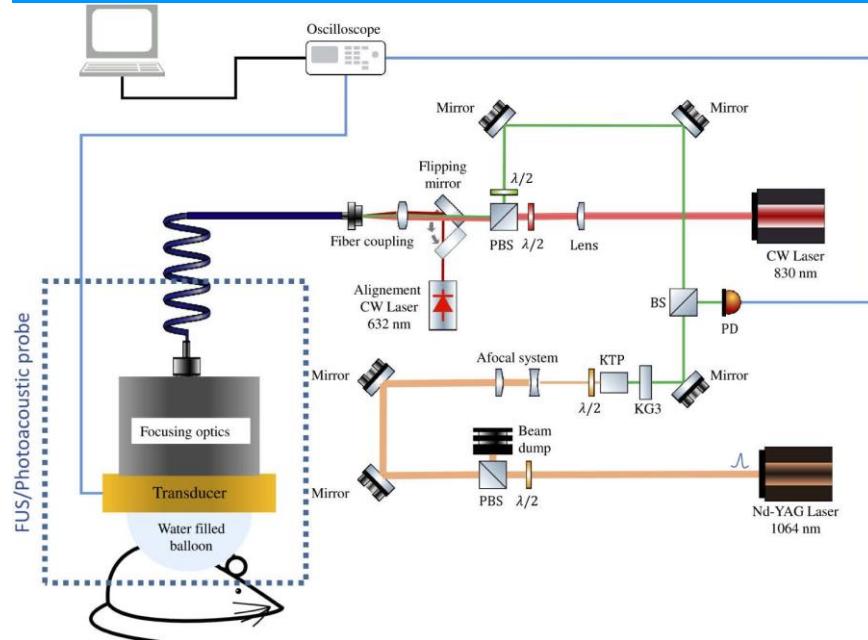


# *Our research in Theranostic*

## 2) R&D in vectorisation and radiolabeling

## Development of a multi-functional preclinical device for the treatment of glioblastoma

### *Blood-brain barrier permeabilization*

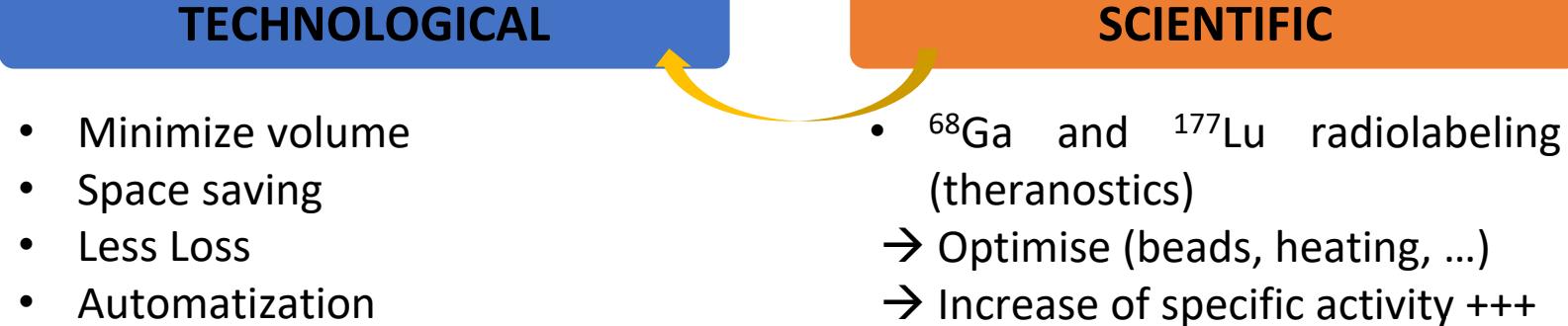


# *Our research in Theranostic*

## 2) R&D in vectorisation and radiolabeling

**Development of automated microfluidics radiosyntheses for molecular theranostics targeting angiogenesis**

MiRTxGlio



**PMB**  
ALCEN



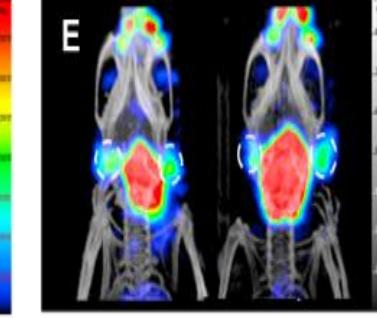
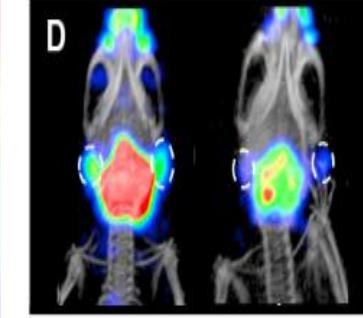
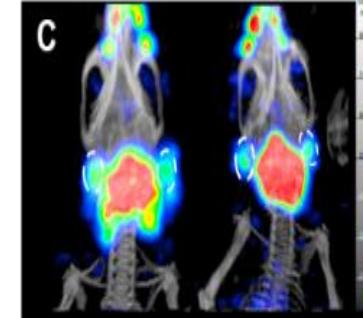
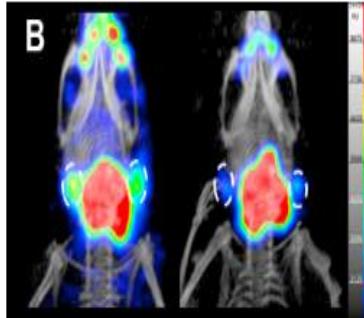
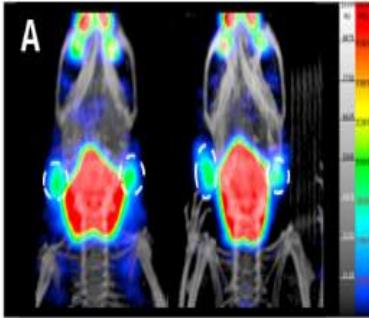
 UNIVERSITY OF Hull  
 Institute Marseille Imaging  
Aix\*Marseille Université

# *Our research in Theranostic*

## 3) Optimization of already validated VIR

Salivary glands and PSMA targeted VIR

Increase therapeutic range of VIR



# *Our research in Theranostic*

In conclusion

2019 : A dedicated M2 Degree



Clinics (1st in man; Phase I → III)

In vivo evaluation

R&D Radiolabelling and medical devices

Vectorization Optimization

Molecular targeted identification





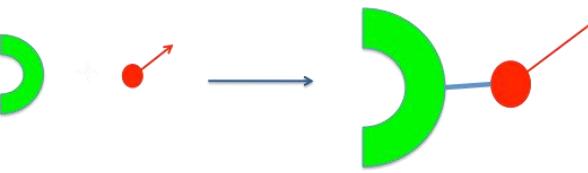
Thanks for your attention



# CERIMED : just box dedicated to R&D in clinical imaging

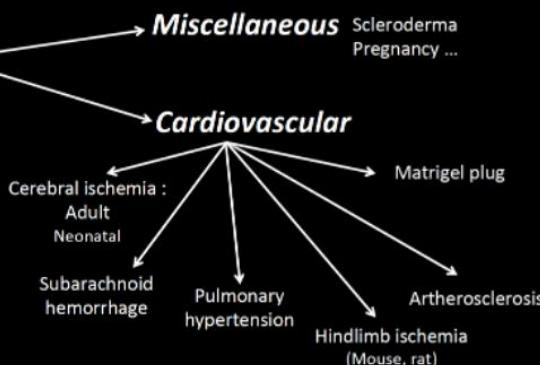


## 1) Radiopharmaceutical platform



## 2) Rodent, swine and monkeys preclinical platform

### Experimental model



### Imaging modalities available

