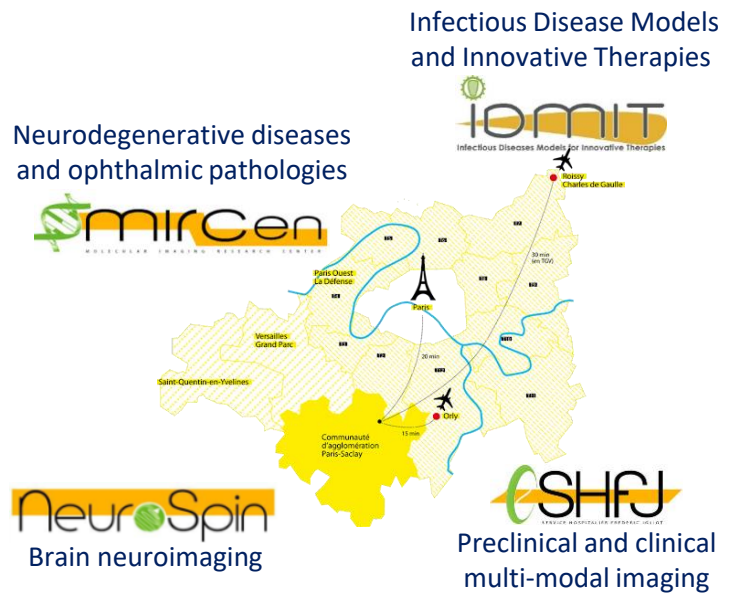


State-of-the-art *in vivo* imaging

RADIOCHEMISTRY ASSETS

A SYNERGY OF IN VIVO IMAGING EXPERTISE & TECHNOLOGIES TO SUPPORT INNOVATIVE PROJECTS

Four complementary and multidisciplinary centers (IDMIT, MIRCen, SHFJ and NeuroSpin) contributing to major advances in various research fields



From preclinical POC to drug development in patients



PET, MRI, ultrasound, multimodal imaging and radiopharmaceutical production

Expertise and state-of-the-art translational in vivo imaging platforms:

- * 4 medical research imaging centers
- * 34 technological platforms for preclinical and clinical research
- * 10 research laboratories

An access to a full range of scientific and technological solutions through one-stop shop and a dedicated project manager to support partner innovative developments from preclinical to clinical stages

ISOTOPES & RADIOPHARMACEUTICALS

OUR ACTIVITY

- ✓ Isotope production (^{11}C , ^{18}F , ^{15}O)
- ✓ Routine synthesis of preclinical and clinical radiopharmaceuticals
- ✓ On demand small (^{11}C , ^{18}F) & large (^{89}Zr , ^{18}F , ^{64}Cu) molecules labeling
- ✓ Multimodal imaging
- ✓ Preclinical and clinical applications

THERAPEUTICAL FIELDS

- ✓ Infectious diseases
- ✓ Neurodegenerative diseases
- ✓ Oncology
- ✓ Addiction
- ✓ Inflammation
- ✓ Ophthalmology

EXPERTISE

- ✓ Preclinical and clinical R&D
- ✓ PET & multimodal imaging
- ✓ Radiotherapy
- ✓ Drugs & biomarkers
- ✓ Labeling methodology

OUR STRENGTH

- ✓ Long-standing experience in radiopharmaceutical and imaging agent development
- ✓ Complementary experts: biologists, physicists, pharmacologists, radiochemists, radiopharmacists, nuclear doctors, physicians
- ✓ A continuum from preclinical to clinical applications to secure the translational research
- ✓ Well-established partnerships with public and industrial players

ISOTOPES

Our offer

Production of radiotracers for biomedical research, in particular for Positron Emission Tomography imaging (PET), from positron emitters produced on site

ISOTOPES

Daily production in house

$^{11}\text{C} / ^{18}\text{F} / ^{15}\text{O}$	Cyclone 18/9 (IBA)
$^{11}\text{C} / ^{18}\text{F}$	iMiTRACE (PBM)

supplied by

^{89}Zr	Perkin
^{64}Cu	Cyrce or Arronax
^{177}Lu	ITM radiopharm



iMiTRACE cyclotron

RADIOSYNTHESIS

^{11}C (6 units)

Mel+ Research	SYNTHRA
TRACERLab FX-C Pro	GE
iPHASE	GE



Radiochemistry laboratory

^{18}F (5 units)

TRACERLab FX-FN	GE
TRACERLab FX-N Pro	GE
All in One	Trasis

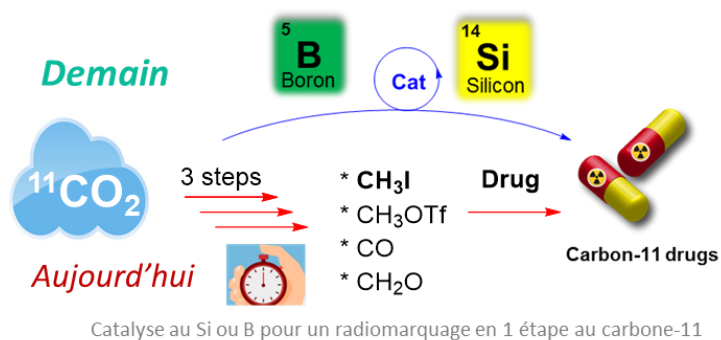


Robotized radiochemistry

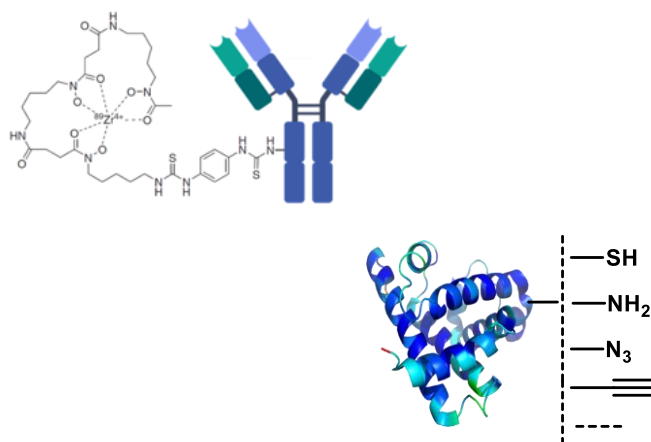
CUSTOM LABELING

Main approaches to develop new tracers

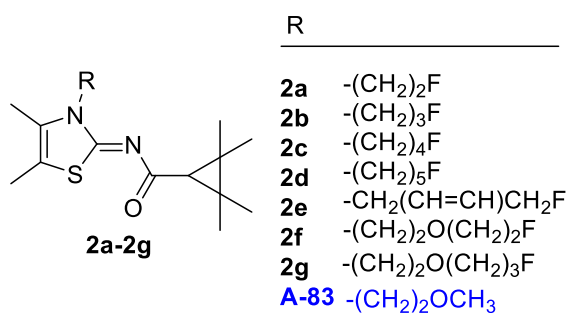
Methodology in ^{11}C and ^{18}F chemistry



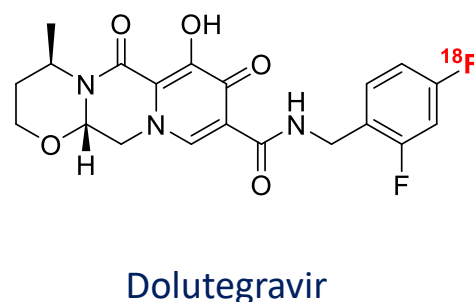
Radiolabelling of biologics



From a scaffold to the tracer



Isotopic labelling of drugs



Modular and versatile approaches for a wide range of radioisotopes

^{11}C - ^{18}F - ^{89}Zr - ^{64}Cu - ^{177}Lu - ^{68}Ga

INNOVATIVE AND VERSATILE RADIOCHEMISTRY

RADIOTRACER PORTFOLIO

	Products	Targets
Used also in clinical tests	[¹⁸ F]DPA714	TSPO
	[¹¹ C]Methionine	Transporters of aa
	[¹⁸ F]fallypride	Dopamine receptors D2/D3
	[¹¹ C]Raclopride	dopamine receptor D2/D3
	[¹¹ C]PE2I	Dopamine Transporter
	[¹⁸ F]AV-1451 (T807)	Tau
	[¹⁸ F]MK6240	Tau
	[¹¹ C]Erlotinib	EGFR
	[¹¹ C]Choline	Oncology
	[¹⁸ F]Fludarabine	Oncology
	[¹¹ C]Buprénorphine	Opioids receptors
	[¹¹ C]Glyburide	Membrane Transporters
	[¹¹ C]Metoclopramide	P-glycoprotein
	[¹¹ C]Flumazenil	GABA-A receptor
	[¹¹ C] PIB	β-amyloid
	[¹⁸ F]FA85380	Nicotinic Ach Receptor
	[¹⁸ F]FC0324	Cannabinoid type 2 receptors
	[¹⁸ F]FET	Transporters of aa
	[¹¹ C]Sorafenib	Tyrosine kinases
	[¹¹ C]Verapamil	Calcium antagonist
[¹¹ C]MeDAS	Myelin	
[¹⁸ F]FPyZide/FPyKyne	Macromolecule labelling	
[¹⁸ F]LBT999	Dopamine Transporter	
[¹⁸ F]FHBG	HSV1-tk reporter - gene therapy	
[¹⁸ F]MNI659	Phosphodiesterase 10	

ON DEMAND MOLECULAR LABELLING

Small molecules < 1000 Da	Preclinical & clinical
Macromolecules > 1000 Da	Preclinical
Protein / Antibody - ⁸⁹ Zr, ¹⁸ F	Preclinical & Clinical



PET APPLICATIONS

PRECLINICAL STAGES

	<i>Examples</i>	LIGANDS	
Characterization/ Validation new ligands	<i>TSPO</i>	DPA714	
	<i>SV2A</i>	UCB-H	
	<i>Tau</i>	T807	
Validation of Models	<i>QA</i>	Fallypride, FDG, MNI659	
	<i>MPTP</i>	(FP), FMT, F-DOPA	
Validation of Therapies	<i>Drug efficacy studies</i>	FDG, F-DOPA	
	<i>Occupancy studies</i>	<i>D2</i>	Fallypride, Raclopride
	<i>Cell replacement in PD / HD</i>		FDG, Fallypride, LBT999, F-DOPA
	<i>Gene therapy</i>		FMT, Fallypride

PET APPLICATIONS

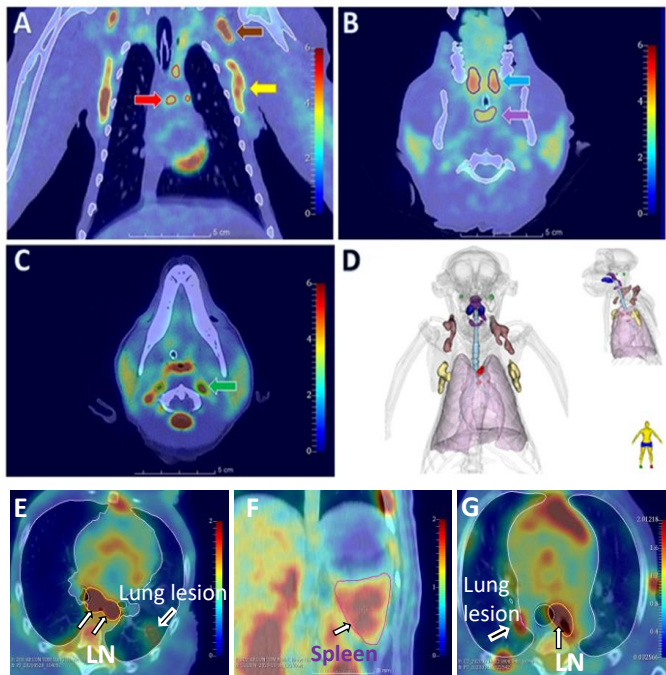
CLINICAL STAGES

Target	Ligand	Pathology
TSPO	DPA-714	Neurology: AD, PD, MS, Epilepsy, Brain Trauma, COVID Psychiatry: Schizophrenia, Bipolar, Autism
SV2A	UCB-J	
Tau	Flortaucipir MK-6240	AD and other dementia
A β Amyloid	PIB (Florbetapir)	AD
Dopaminergic pathway : Post synaptic receptor	Raclopride Fallypride	HD, PD
	Pre-synaptic transporter	PD, Addiction
	Dopamine synthesis	
	PE2I LBT-999	
	F-DOPA	
Nicotinic ACh Receptor	F-A85380	AD, Addiction, Epilepsy, PD
P-glycoprotein	metoclopramide	Epilepsy, AD
GABA _A receptor	Flumazenil	MS
Opioid receptor	Buprenorphin	Pharmacology

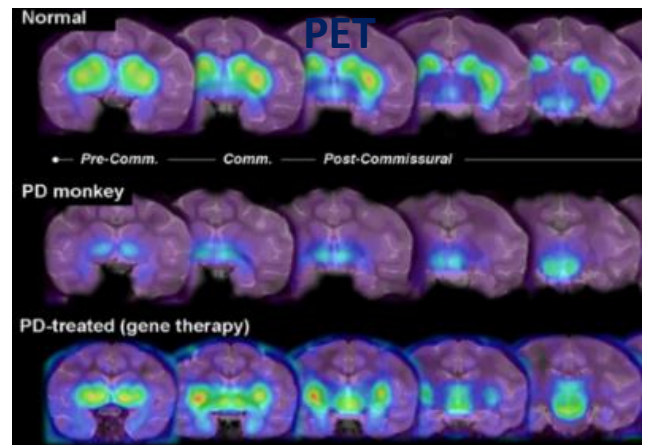
AD: Alzheimer's disease
 PD: Parkinson's disease
 HD: Huntington's disease
 MS: Multiple Sclerosis

PRECLINICAL CASE STUDIES

PET-CT



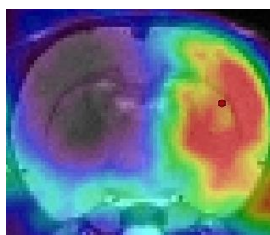
Infection effect of Sars-Cov-2 –
[¹⁸F]FDG uptake
Lemaitre et al., Mol. Immunology 2021



Gene therapy efficacy on an animal model of
Parkinson's disease - [¹⁸F] 6-FMT
Aron Badin et al., Mol Ther Methods Clin Dev. 2019

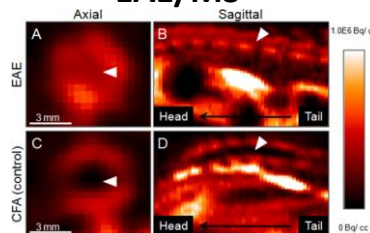
PRECLINICAL VALIDATION OF [¹⁸F]DPA-714

Stroke



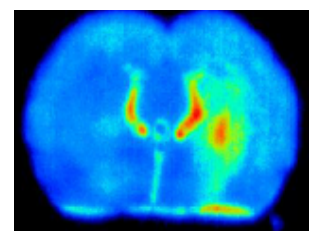
Martin et al., 2010

EAE/MS



Abourbeh et al., 2012

Kainate inj.

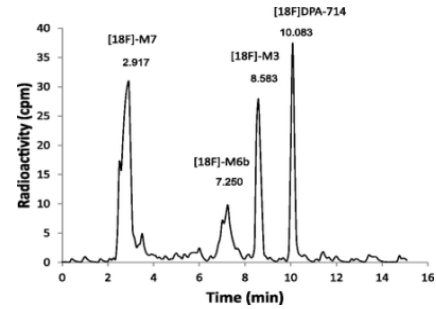
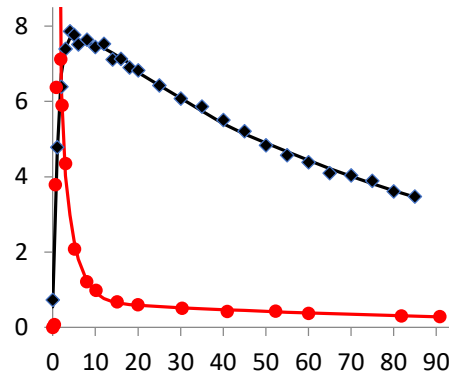
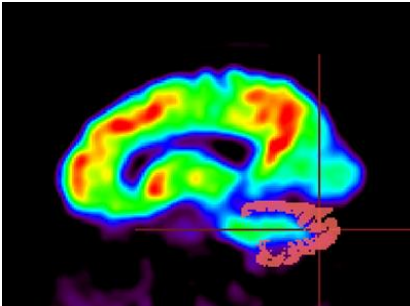


Chaveau et al., 2009

Animal models of neuroinflammation using [¹⁸F]DPA-714 binding TSPO, a biomarker of microglia activation

CLINICAL CASE STUDIES

QUANTIFICATION STUDY OF [¹⁸F]DPA-714 IN HEALTHY SUBJECT



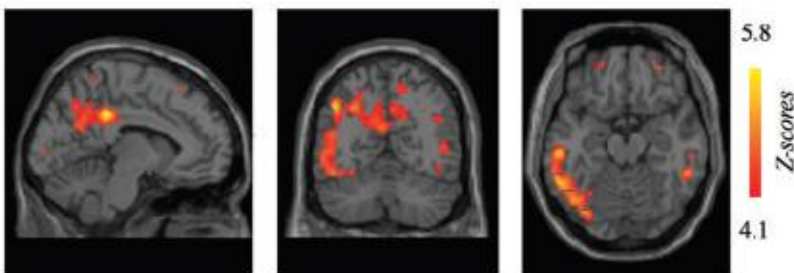
Lavisse et al., 2015 ; Garcia-Lorenzo et al., 2018; Wimberley et al., 2018; Peyronneau et al., 2013

Cerebellum TSPO (a marker of microglia) imaging using [¹⁸F]DPA-714

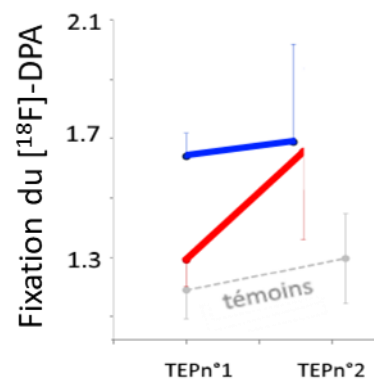
Kinetic profiling of metabolites in brain (blue) and plasma (red)

LONGITUDINAL STUDY OF THE MICROGLIAL ACTIVATION IN AD

TSPO IMAGING ¹⁸F-DPA-714 :
Alzheimer patients > Controls



Hamelin et al., Brain 2016 ; 2018



Temporo-parietal cortex imaging: [¹⁸F]DPA-714 binding was higher in patients with AD than in controls in all volumes of interest

Individual analysis showed heterogeneous [¹⁸F]DPA-714 binding progression profiles among patients with AD (blue compared to red)



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