PASREL imagerie

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

Infectious Disease Models and Innovative Therapies

Neurodegenerative diseases and ophthalmic pathologies

Brain neuroimaging

Preclinical and clinical multi-modal imaging

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 (rodents and non-human primates) 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
- ✓ Rodents & Non-human primates
- ✓ 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

Organic synthesis for the preparation of radiolabeling precursors

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

Chemistry	
Multi-step synthesis for customized preparation of reference compounds and radiolabeling precursors	
Solutions for the radiolabeling of biologics	

Chemistry laboratory

Cyclone 18/9 (IBA)

ISOTOPES	
Daily production in house	
^{11}C / ^{18}F / ^{15}O	Cyclone 18/9 (IBA)
supplied by	
^{89}Zr	Reviity
^{64}Cu	Cyrce or Arronax
^{177}Lu	ITM radiopharm

RADIOTRACERS AND RADIOPHARMACEUTICALS

PRECLINIAL RADIOSYNTHESIS	
^{11}C (3 units)	
MeI+ Research	SYNTHRA
iPHASE	GE
^{18}F (3 units)	
All in One	Trasis

Radiochemistry laboratory

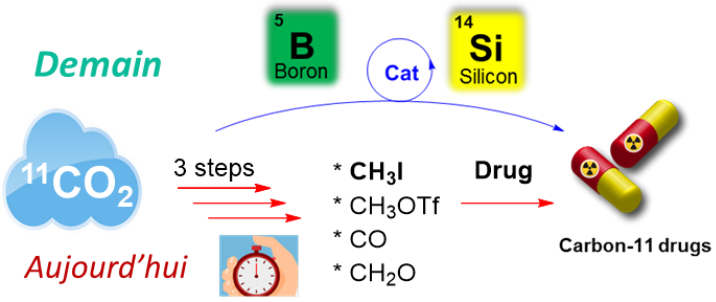
CLINICAL MANUFACTURING	
^{11}C (2 units)	
iPHASE	GE
^{18}F (2 units)	
All in One	Trasis

GMP manufacturing

CUSTOM LABELING

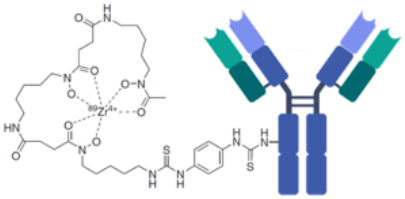
Main approaches to develop new tracers

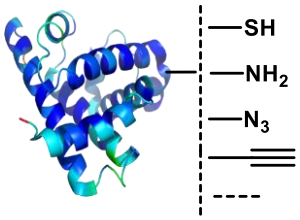
Methodology in ^{11}C and ^{18}F chemistry



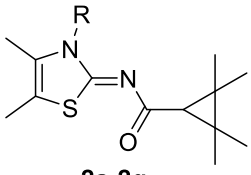
Catalyse au Si ou B pour un radiomarquage en 1 étape au carbone-11

Radiolabelling of biologics





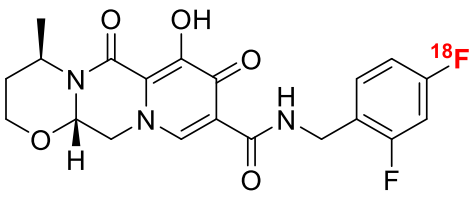
From a scaffold to the tracer



2a-2g

R	
2a	$-(CH_2)_2F$
2b	$-(CH_2)_3F$
2c	$-(CH_2)_4F$
2d	$-(CH_2)_5F$
2e	$-CH_2(CH=CH)CH_2F$
2f	$-(CH_2)_2O(CH_2)_2F$
2g	$-(CH_2)_2O(CH_2)_3F$
A-83	$-(CH_2)_2OCH_3$

Isotopic labelling of drugs



Dolutegravir

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
	^{1}C]Metoclopramide	P-glycoprotein
	[^{11}C]Flumazenil	GABA-A receptor
	[^{11}C] PIB	β-amyloid
	[^{18F}]FA85380	Nicotinic Ach Receptor
	[^{18F}]FC0324	Cannabinoid type 2 receptors
	[^{18F}]FET	Transporters of aa
	[^{11}C]Sorafenib	Tyrosine kinases
	[^{11}C]Verapamil	Calcium antogonist
	[^{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

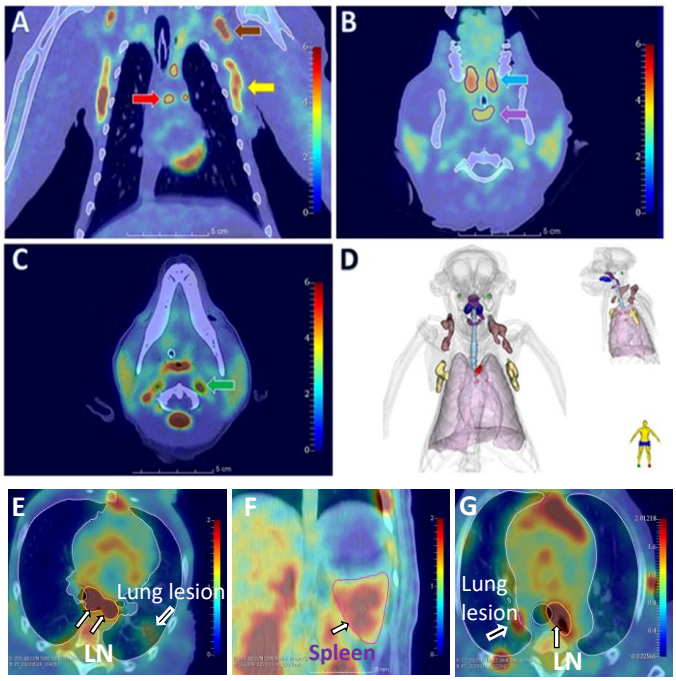
Small molecules < 1000 Da	Preclinical & clinical
Macromolecules > 1000 Da	Preclinical
Protein / Antibody - ^{89}Zr, ^{18}F	Preclinical & Clinical

PRECLINICAL PET APPLICATIONS

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

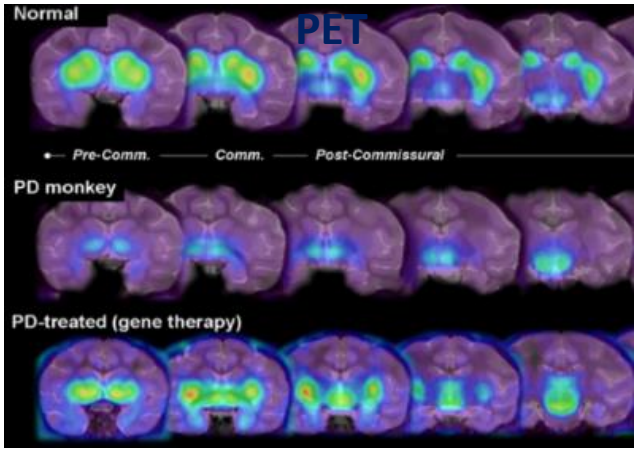
PRECLINICAL CASE STUDIES

PET-CT



Infection effect of Sars-Cov-2 in NHP - [^{18}F]FDG uptake

Lemaitre et al., Mol. Immunology2021

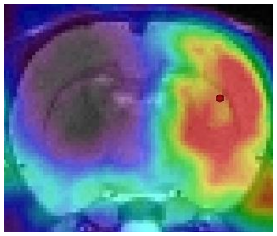


Gene therapy efficacy on a NHP model of Parkinson's disease - [^{18}F] 6-FMT

Aron Badin et al., Mol Ther Methods Clin Dev. 2019

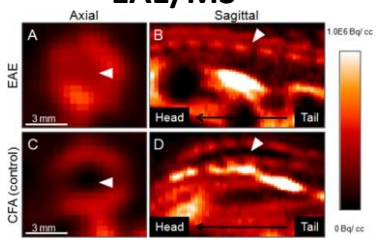
PRECLINICAL VALIDATION OF [^{18}F]DPA-714

Stroke



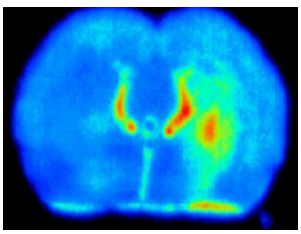
Martin et al., 2010

EAE/MS



Abourbeh et al., 2012

Kainate inj.



Chaveau et al., 2009

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

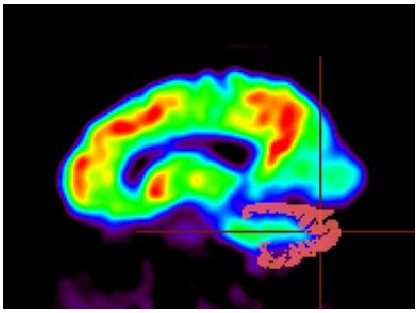
CLINICAL PET APPLICATIONS

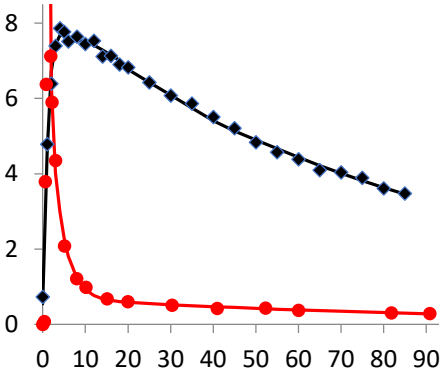
Target	Ligand	Pathology
TSPO	DPA-714	Neurology: AD, PD, MS, Epilepsy, Brain Trauma, COVID Psychiatry: Schizophrenia, Bipolar, Autism
SV2A	UCB-J	
Tau	Flortaucipir MK-6240	AD and other dementia
Aβ Amyloid	PIB (Florbetapir)	AD
Dopaminergic pathway : Post synaptic receptor	Raclopride Fallypride	HD, PD
Pre-synaptic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

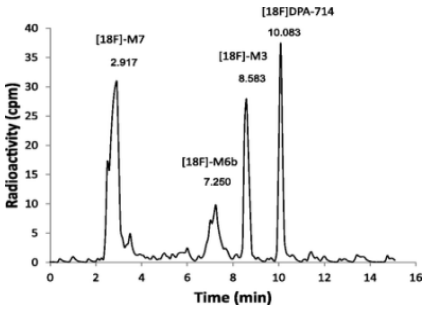
AD: Alzheimer's disease
PD: Parkinson's disease
HD: Huntington's disease
MS: Multiple Sclerosis

CLINICAL CASE STUDIES

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







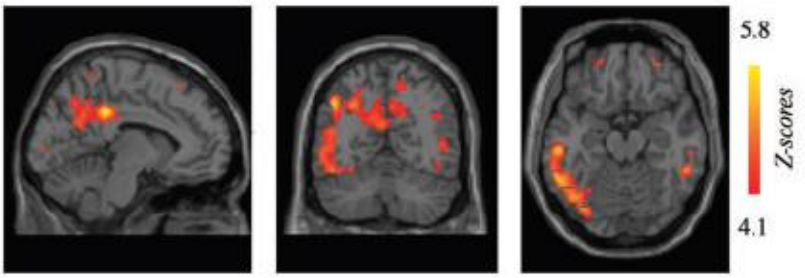
Lavisse et al., 2015 ; Garcia-Lorenzo et al., 2018; Wimberley et al., 2018; Peyronneau et al., 2013

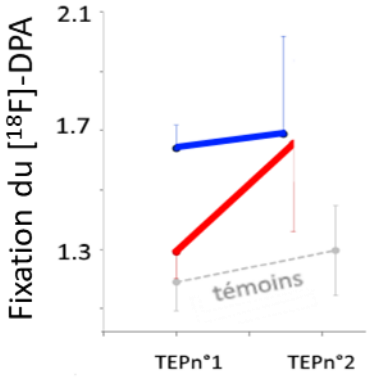
Cerebellum TSPO (a marker of microglia) imaging using [^{18}F]DPA-714

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

LONGITUDINAL STUDY OF THE MICROGLIAL ACTIVATION IN AD

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





Hamelin et al., Brain 2016 ; 2018

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

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

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