Groupement de recherche

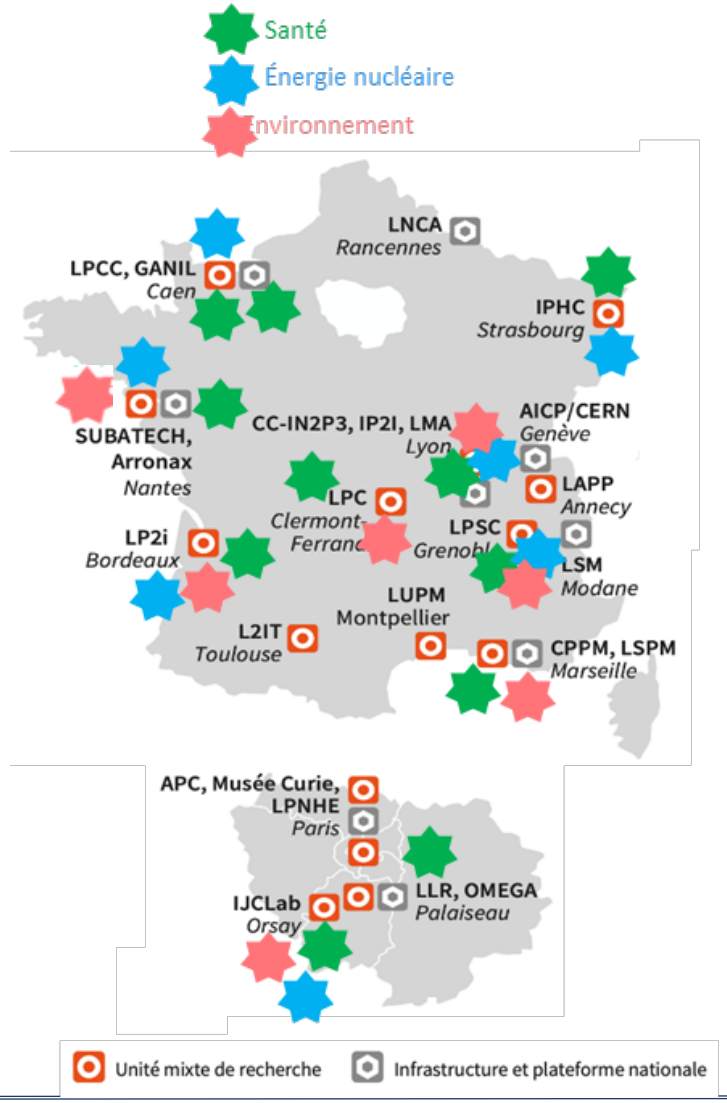
MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

Overview of Health-related activities at IN2P3 (CNRS- Nucléaire & Particules)

ML Gallin-Martel LPSC Grenoble

Lyon, July 8, 2025 Conseil Scientifique IN2P3

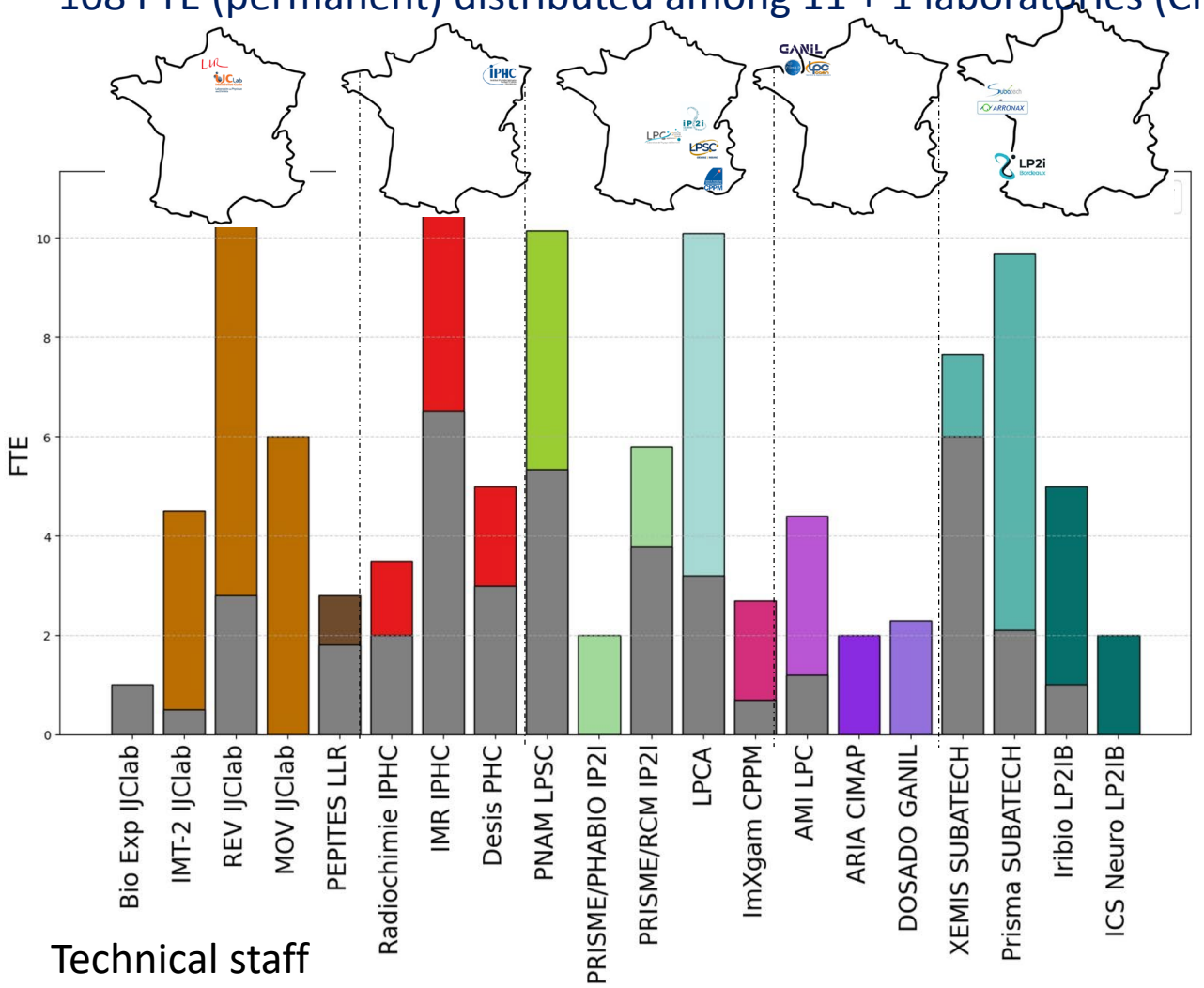
IN2P3 : Interdisciplinary Research for Health

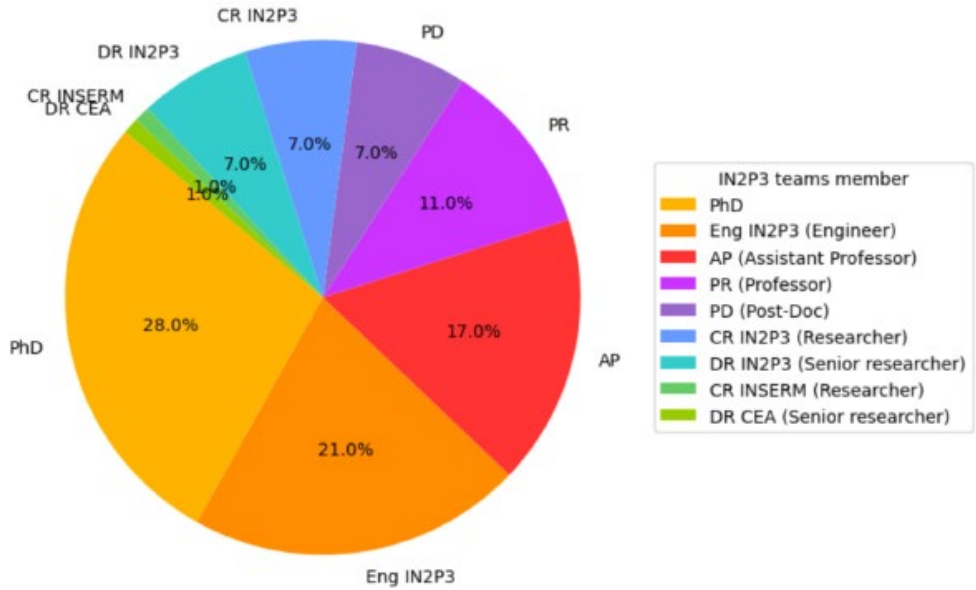


- **Key Figures (2015–2024):**
  - 11 (+1 CIMAP) IN2P3 laboratories
  - ~75 permanent researchers
  - ~60 PhDs & postdocs

Human resources

~108 FTE (permanent) distributed among 11 + 1 laboratories (CIMAP)





Technical staff

Researchers

High proportion of non-permanent staff, including engineers on fixed-term contracts, and “teacher-researchers”

IN2P3 : Interdisciplinary Research for Health

Main Research Axes:

- Imaging

➢ **High sensitivity multimodal diagnostic imaging:**
- PET, ToF-PET (e.g. ClearMind), PET/CT and PET/MRI,
- X-ray Photon-Counting CT
- 3-gamma imaging (e.g. XEMIS2)

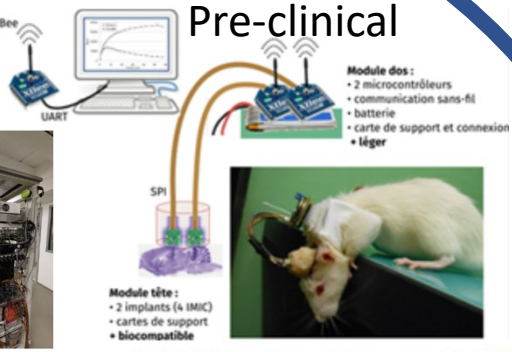
➢ **Preclinical imaging:**
- Demonstrators (e.g. PIXSCAN)
- Intracranial probes for imaging in awake animals (e.g. MAPSSIC)

➢ **Clinical imaging:** image-guided therapy
- Intraoperative imaging in surgery (e.g. OPALIS)

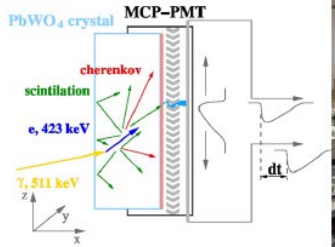
Imaging

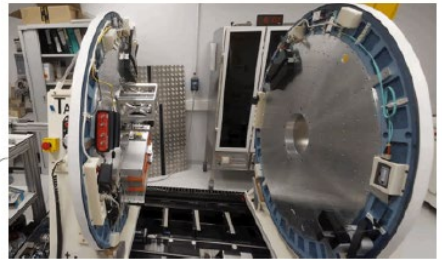
XEMIS2, CHU Nantes
pre-clinical

MAPSSIC
Pre-clinical



ClearMind - clinical



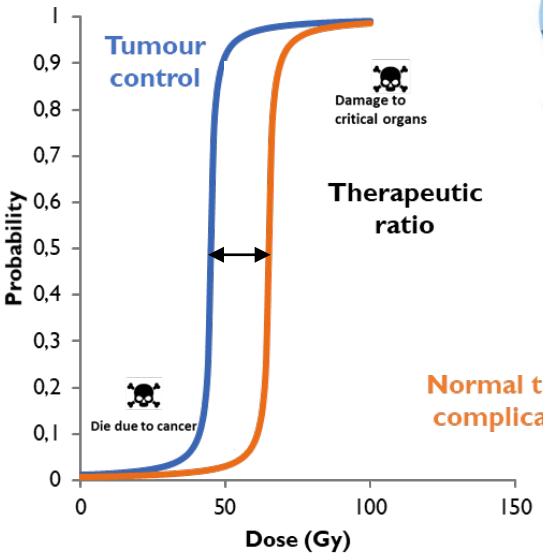


Intraoperative endomicroscope
OPALIS - clinical

IN2P3 : Interdisciplinary Research for Health

Main Research Axes:

- Imaging
- Radiotherapy -> RadiotherapIES

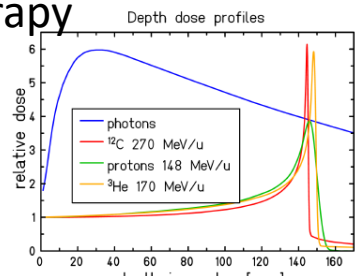


One of the **main objectives** is **to widen this therapeutic window** to increase the differential response between tumor tissues / healthy tissues

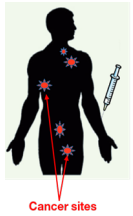
The dose unit is Gy = 1 J/kg

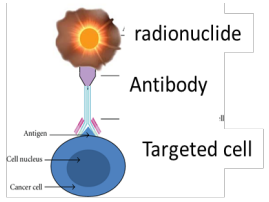
Radiotherapies

X rays / Hadrontherapy

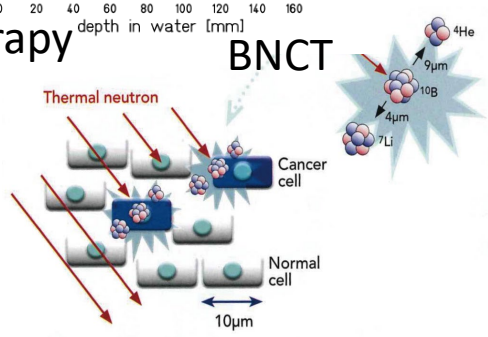


Targeted Radionuclide Radiotherapy

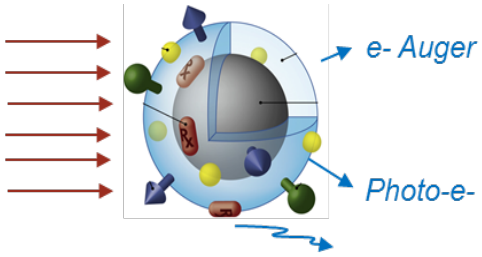




BNCT



Nanoparticles



IN2P3 : Interdisciplinary Research for Health

- **Main Research Axes:**
  - Imaging
  - Radiotherapy
  - Radiobiology

Radio-resistant tumor models / normal cells: in vitro studies with cell lines / organoids / eggs/animals

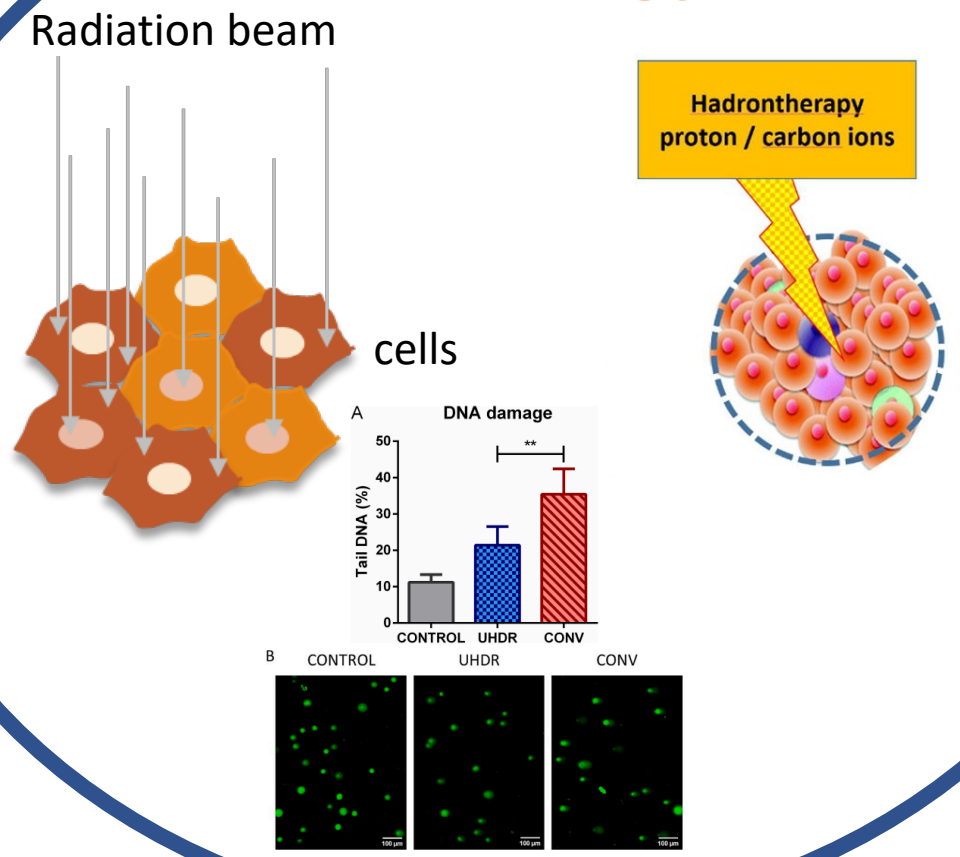
Innovative combinations: use of targeted radio-sensitizers

Interest of carbon ions?

Interest of Ultra High Dose Rate (UHDR) = FLASH?

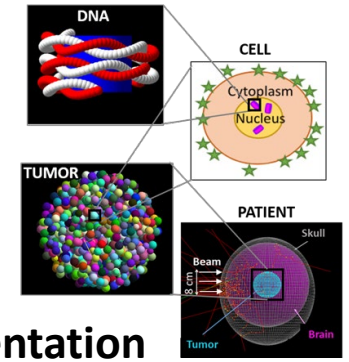
Basic biol/chem mechanisms of therapeutic efficacy…

Radiobiology



IN2P3 : Interdisciplinary Research for Health

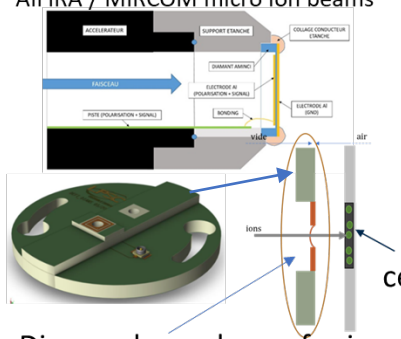
Physics for Radiobiology



Multi scale
Modeling
Tools

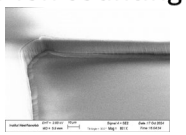
Beam monitor instrumentation

AIFIRA / MIRCOM micro ion beams

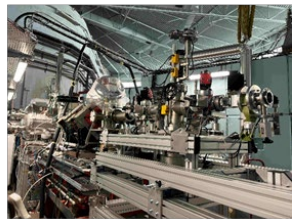


cells

Diamond membrane for ion counting



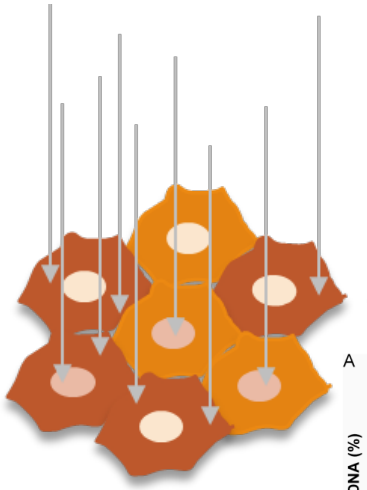
ALTO



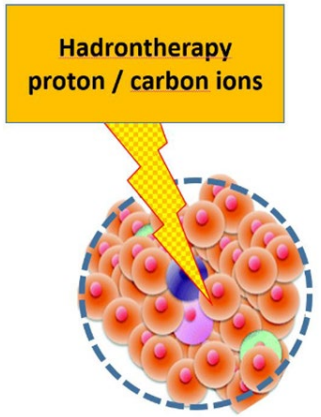
Diamond beam monitor

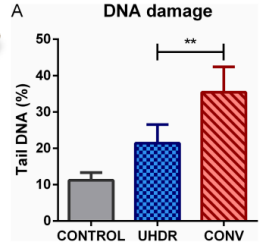
Radiobiology

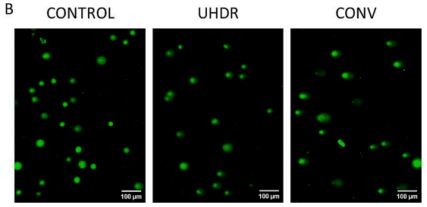
Radiation beam



cells







IN2P3 : Interdisciplinary Research for Health

Main Research Axes:

- Imaging
- Radiotherapy
- Radiobiology
- Radionuclides

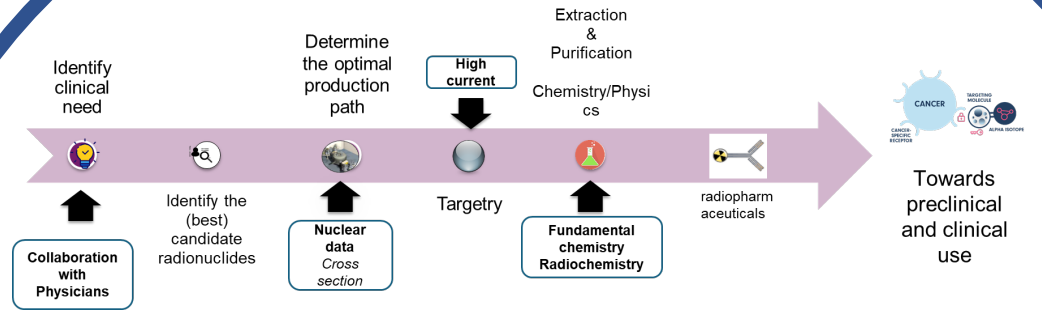
Production issues:

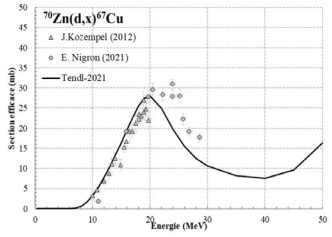
- **quantitative**: beams, targets,
- **qualitative**: purity, separation.

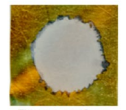
Key parameters:

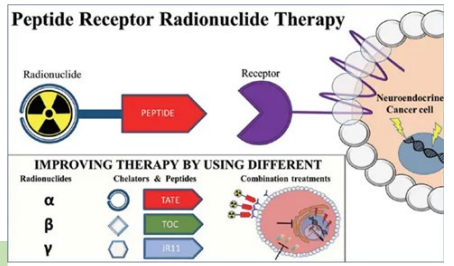
- **Radiation type** → depends on application (Imaging vs Therapy)
- **Half-life** → to match **biodistribution time**
- **Chemical properties** → to ensure **stable attachment** to vector molecule

Radionuclides









Applications:
Alpha therapy
Auger Therapy
Theranostic
µ-dosimetry
Radiolysis
Radiobiology

Numerous radionuclides have emerged:

- β^+ emitters: ^{64}Cu, ^{68}Ga, ^{89}Zr …
- γ emitters: ^{97}Ru, ^{155}Tb, ^{203}Pb …
- β^- emitters: ^{161}Tb, ^{166}Ho, ^{177}Lu …
- α emitters: ^{211}At, ^{212}Bi, ^{213}Bi, ^{223}Ra, ^{225}Ac …
- Auger: ^{103}Ru, ^{117m}Sn, ^{123}I, ^{155}Tb …
- Theranostic pairs: ^{44}Sc/^{47}Sc, ^{64}Cu/^{67}Cu, ^{68}Ga/^{177}Lu …

New radiopharmaceuticals have been approved

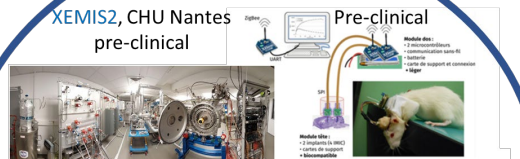
- For diagnosis (γ, β^+)
  Detecnet (^{64}Cu) by FDA in the USA: imaging of NET
- For targeted therapy (β^-)
  Lutathera (^{177}Lu) by FDA and EMA: NET
  Pluvicto (^{177}Lu) by FDA and EMA: prostate cancer

IN2P3 : Interdisciplinary Research for Health

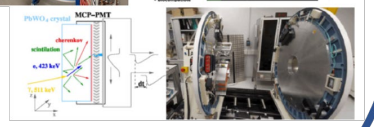
Imaging

XEMIS2, CHU Nantes pre-clinical

MAPSSIC Pre-clinical



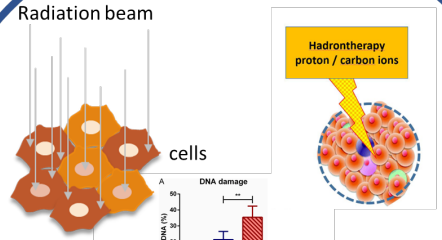
ClearMind - clinical



Intraoperative endomicroscope OPALIS - clinical

Radiobiology

Radiation beam



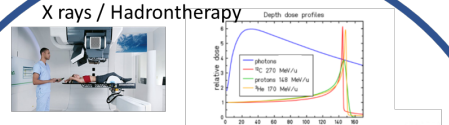
Scientific Objectives

Using ionizing radiation to **understand their effect on living matter** and participate to the **development of therapeutic applications** against cancer.

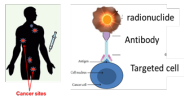
RadiationS for Health

Radiotherapies

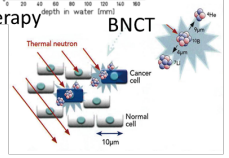
X rays / Hadrontherapy



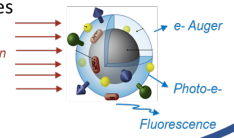
Targeted Radionuclide Radiotherapy



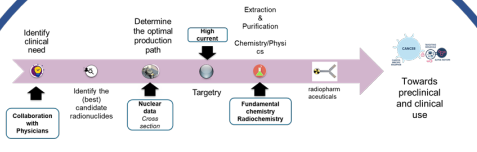
BNCT

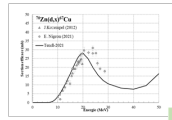


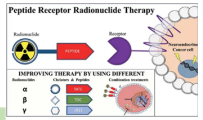
Nanoparticles



Radionuclides







Applications:
Alpha therapy
Auger Therapy
Theranostic
µ-dosimetry
Radiolysis
Radiobiology

Expertise areas

- In relation with nuclear physics, radiochemistry, detector development, Monte-Carlo simulation tools, mastering complex experiments, accelerators:
  - **Multi-scale simulation tools** (GATE, Geant4-DNA, NanOx)
  - **Innovative imaging** (ToF-PET, SPECT, X-ray Photon Counting CT, Compton imaging, proton radiography, non linear optical imaging)
  - **Innovative radiotherapies**: Hadrontherapy, FLASH, Micro Beams, Targeted Therapies, …
    - irradiation beamline developments
    - online beam monitoring,
    - dosimetry
    - secondary particle imaging
  - **Radionuclides production**
  - **Physics developments** (modeling and beam instrumentation) **to support research in radiobiology**

Positioning

- **Expertise in modeling:** leadership in highly-used **open-source code**
- **Expertise in instrumentation => developments** with the objective of delivering:
  - demonstrators supporting the **emergence of disruptive technologies**,
  - **as part of a strategic technological watch,**
  - **finalized applications.** → Clinical transfer

→ Research

- **Unique irradiation platform network (RESPLANDIR) to carry out research activities**

National and local collaborations

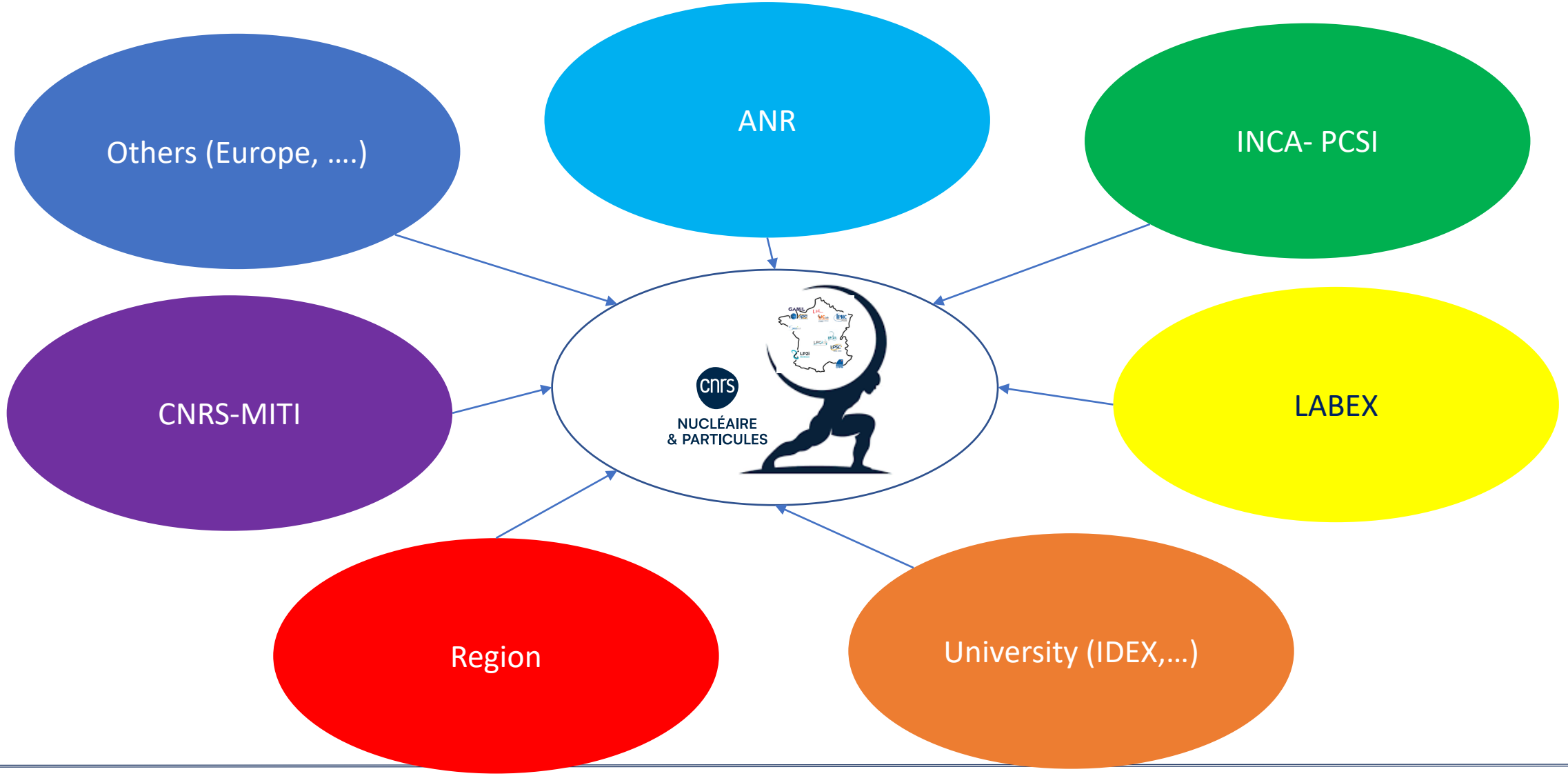
- **Biologists & clinicians integrated in IN2P3 labs** (e.g. LP2IB, IP2I Lyon, IJClab, LPCA, IPHC)
- **Partnerships:**
  - **Existing**: IN2P3 – CAL (Hadrontherapy Center Antoine Lacassagne in Nice), IN2P3-ASNR (formerly IRSN), IN2P3-Inserm
  - **Other under discussion**: **IN2P3 – CYCLADE** (ARCHADE Advanced Resource Centre for Hadrontherapy In Europe program) hadrontherapy center in Caen
- **Local collaboration: CHU** and with **cancer treatment centers** (e.g in Orsay Institut Curie, Institut Gustave Roussy, …)
- **GDR MI2B** created by IN2P3 (in 2004 G Montarou LPCA IN2P3 and P. Mangeot DAPNIA CEA), **now a CNRS-wide initiative**
  - Involves **CNRS (Biology, Physics, Engineering, Computer Science), Inserm, …**
  - Partnerships with **SFPM, SFBR, and national platforms (e.g. ALTO, AIFIRA, ARRONAX, GANIL, CYRCé)**

International collaborations

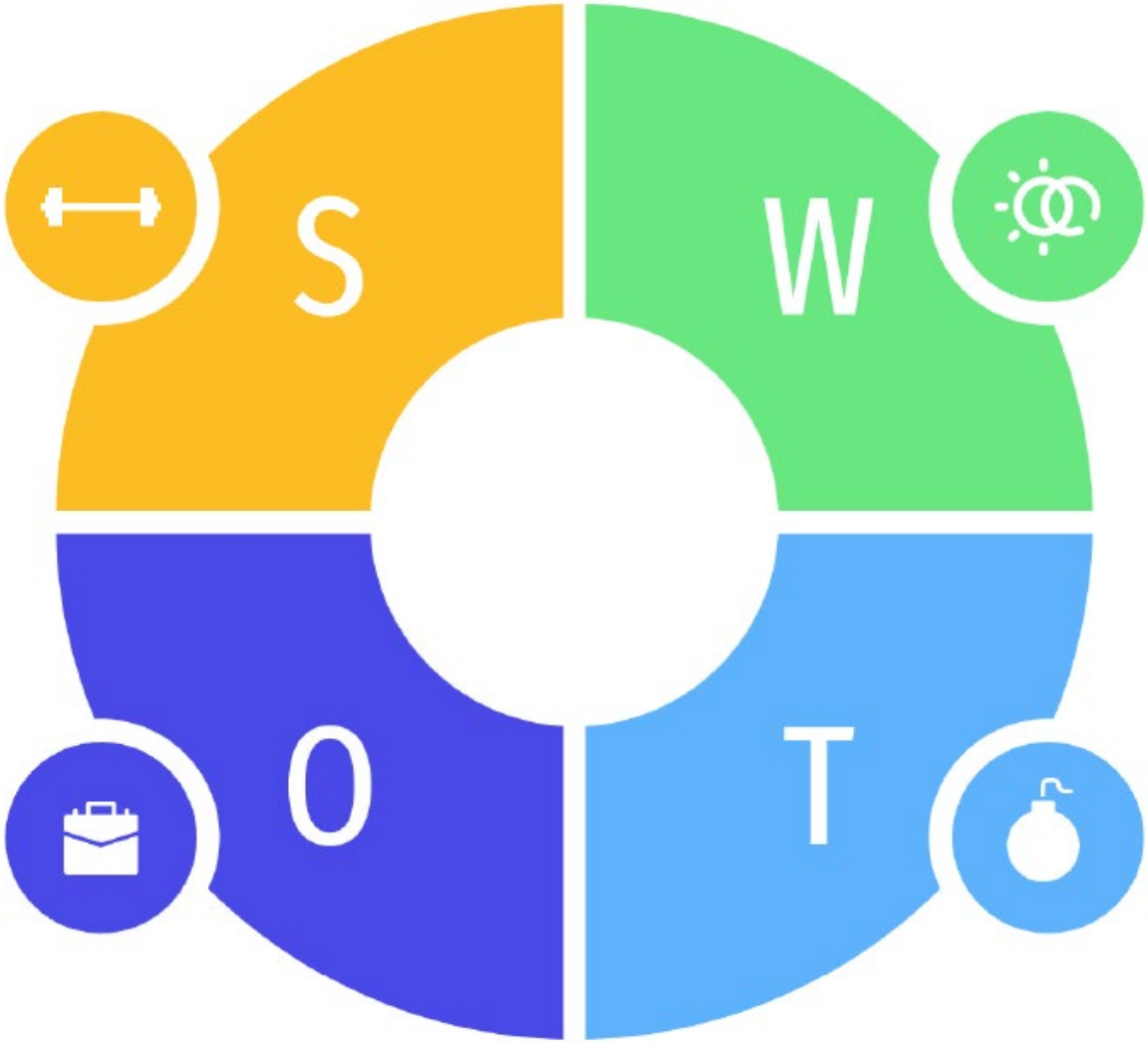
- **Multi-scale simulation tools** (GATE, Geant4-DNA, NanOx)
- **Innovative imaging** (ToF-PET, SPECT, Compton imaging, proton radiography)
- **Innovative radiotherapies**: Hadrontherapy, FLASH, Micro Beams, targeted therapies, …
  - irradiation beamlines development
  - online beam monitoring,
  - dosimetry
  - secondary particle imaging
- **Particle and radionuclide production**
- **Radiobiology**

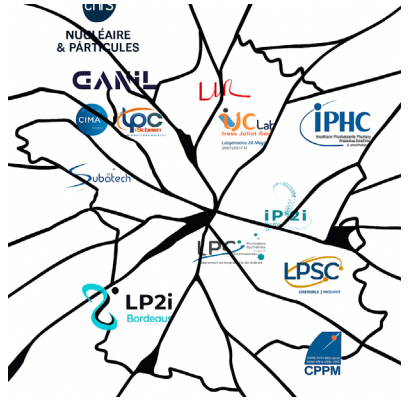
Country	Institution	Topic
EU	PRISMAP, EURADOS	Radionuclide production, dosimetry
Italy	INFN	FOOT-Xn (FOOT collaboration), radionuclide production
	CNAO	FOOT-Xn, ANR CLINM, carbon radiobiology
Switzerland	CERN, CERN MEDICIS	imXgam: R&D detector, radionuclide production
Spain	University of Seville	Radionuclide production
	University of Granada	BNCT modeling
	CSIC Valencia	R&D Compton camera
Belgium	Univ. Leuven	Proton FLASH
UK	Imperial College	Lhara: laser acceleration for medical use
Germany	GSI	Hadrontherapy monitoring with CMOS sensors
Poland	IFJ PAN	Radiobiology, dosimetry
Argentina	University of Rosario	Atomic and molecular theoretical physics
	CNEA Buenos Aires	BNCT
Australia	Ansto	Microbeam radiotherapy
Japan	NIRS	Radiobiology
	AIST, Tsukuba	Diamond detectors
South Korea	Cath. Univ. Of Korea	Compton Imaging
	Korea Atomic En. Res. Inst.	
USA	NASA	IEA project: DNA break modeling for space research

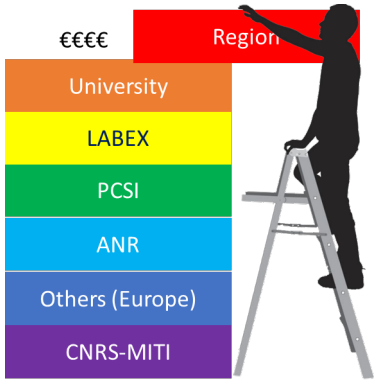
The budget


Others (Europe, ….)
ANR
INCA- PCSI
CNRS-MITI
NUCLÉAIRE & PARTICULES
LABEX
Region
University (IDEX,…)

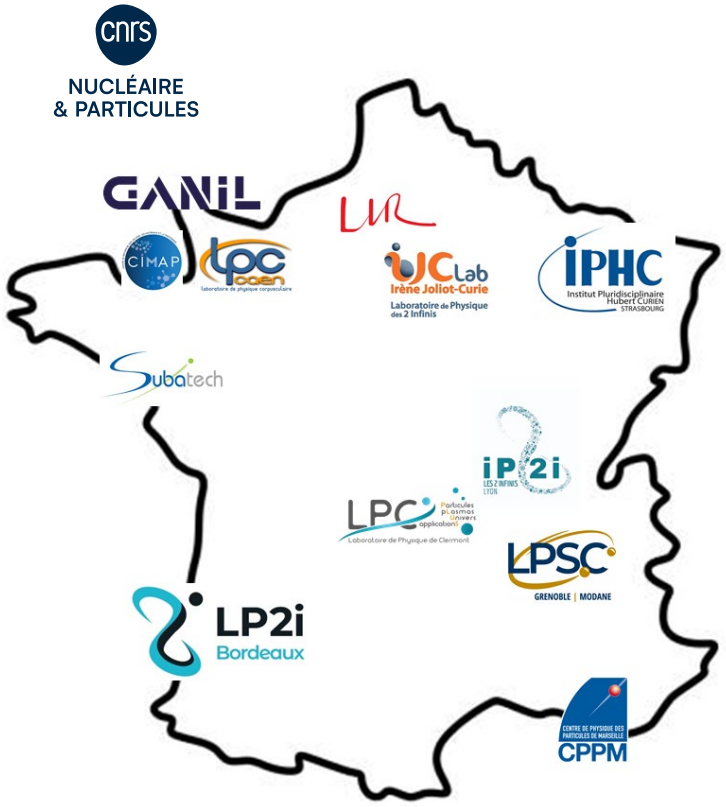
Project-based structuring







GDR MI2B

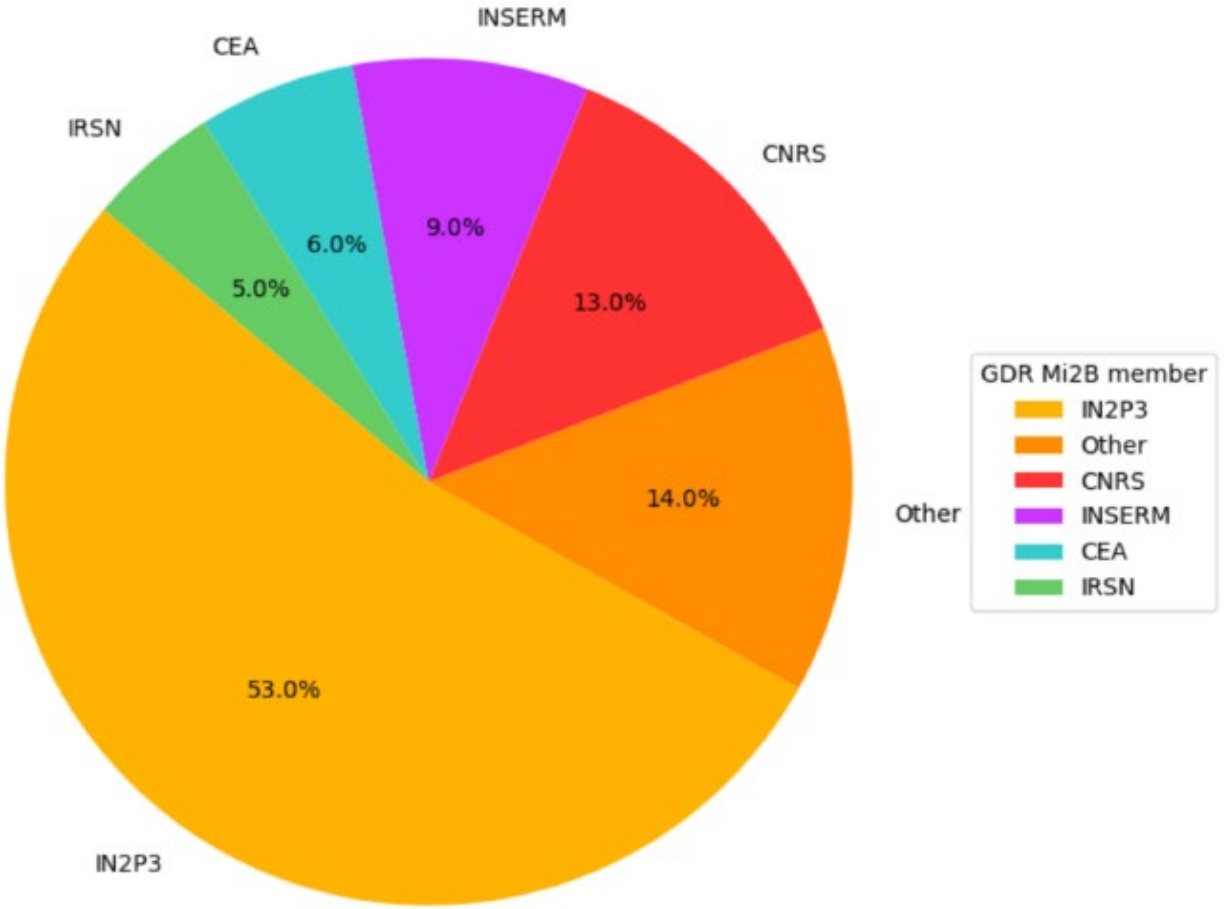


- **The GDR MI2B**: a scientific **coordination research group**
- Open to **CNRS- Biology** teams (deputy management), but also to **CNRS Engineering**, **CNRS Physics**, **CNRS Computer Sciences**, **Inserm**, **ASNR**, …
- **36** partner teams, including:
  - **12 IN2P3** (CNRS Nuclear & Particle Physics)

    + platforms:
    AIFIRA (Bordeaux) – **CYRCÉ** (Strasbourg) – **ALTO** (Orsay) – **Arronax** (Nantes) – **GANIL** (Caen)
  - **11 CNRS Biology**

=> ~280 subscribers to the mailing list

GDR MI2B members



Largely open to other institutes working in the field of health, with a majority from IN2P3 which initiated its creation

Research Areas and Cross-cutting Themes

4 Key Research Areas or Domains

Methods and Instruments in Biomedical Imaging

Tools and Physical Methods for Innovative Radiotherapies

Effects of Radiation on Living Organisms

Radionuclides for Imaging and Therapy

Research Areas and Cross-cutting Themes

Methods and Instruments in Biomedical Imaging

- **High-sensitivity multimodal diagnostic imaging** (PET, PET/CT and PET/MRI, X-ray PC-CT, 3-gamma imaging, …)
- **Treatment planning** (proton tomography)
- **Image-guided therapy** (prompt gamma imaging for dose delivery monitoring in hadron therapy, intraoperative imaging in surgery)
- **Preclinical imaging** (demonstrators, multimodal platforms, simultaneous hybrid imaging, intracranial probes for imaging in awake animals)

Research Areas and Cross-cutting Themes

Tools and Physical Methods for Innovative Radiotherapies

- **Improving the therapeutic index of radiation treatments**
  ⇒ Increase the probability of tumor control without increasing complications to healthy tissues.
- **Quality control of treatment delivery**
- **Innovative dose delivery methods** *(energy, position, timing)*
- **Optimization of treatment planning**

Research Areas and Cross-cutting Themes

Effects of Radiation on Living Organisms

- **Understanding the mechanisms involved in low-dose exposure**
- **Contributing to the challenges of modeling living systems and associated predictive models**
- **Studying radiolysis of water and biomolecules**
- **Assessing changes at different scales** *(molecular, cellular, whole body)*
- **Understanding the mechanisms involved in therapeutic exposures**
- **Optimizing conventional radiotherapy protocols and developing innovative therapies**
- **Estimating radiation risk associated with each modality**

Research Areas and Cross-cutting Themes

Radionuclides for imaging and therapy

- The challenge is **to stimulate research related to innovative radionuclides in a theranostic approach** (combining imaging and therapy).
- The main questions addressed in this context are:
  - **Which innovative radionuclides should be promoted?**
  - **Which biological agents are suitable for selective delivery?**
  - **How can we produce these radionuclides with suitable purity and quantity for medical applications**
  - **How can the radionuclide be stably attached to the biological vector?**

Research Areas and Cross-cutting Themes

4 Key Research Areas or Domains

Methods and Instruments in Biomedical Imaging

High-sensitivity multimodal diagnostic imaging (PET, PET/CT and PET/MRI, X-ray PC-CT, 3-g

Treatmen tomography)

Image-gu (prompt g dose deli hadron th intraoperat surgery)

Preclinica (demonst platforms hybrid im probes for imaging in awake animals)

Tools and Physical Methods for Innovative Radiotherapies

Improving the therapeutic index of radiation treatments
⇒ Increase the probability of

Effects of Radiation on Living Organisms

Understanding the mechanisms involved in low-dose exposure

Contributing to the challenges of modeling living systems

Estimating radiation risk associated with each modality

Radionuclides for imaging and therapy

The challenge is **to stimulate research related to innovative radionuclides in a theranostic approach** (combining imaging

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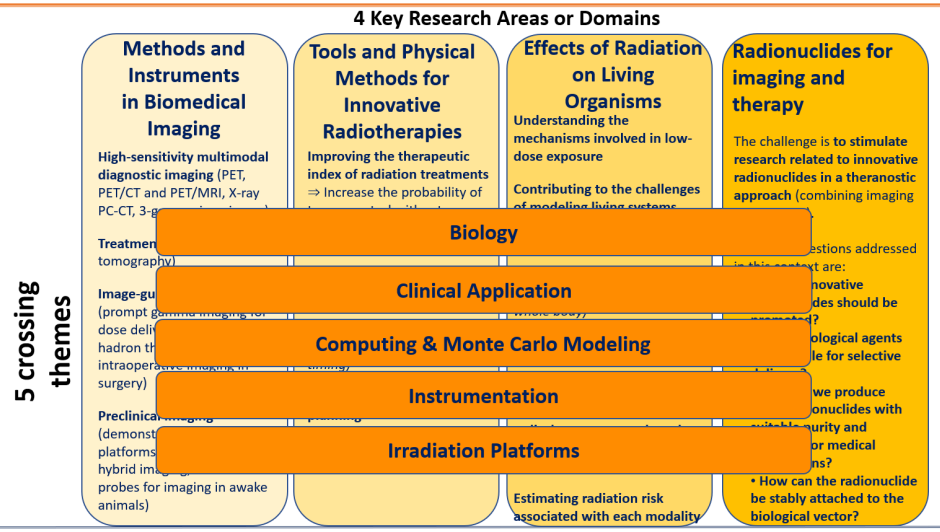
- **How can the radionuclide be stably attached to the biological vector?**

5 crossing themes

- **Biology**
- **Clinical Application**
- **Computing & Monte Carlo Modeling**
- **Instrumentation**
- **Irradiation Platforms**

GDR MI2B Governance

Research Areas and Cross-cutting Themes



Direction
Marie-Laure Gallin-Martel
(LPSC – IN2P3)
Lucie Sancey
(IAB – CNRS Biology)

Division Heads

Imaging
Marc-Antoine Verdier (IJClab- IN2P3)
Mathieu Dupont (CPPM – IN2P3)

Radiotherapies
Rachel Delorme (LPSC-IN2P3)
Jean-Michel Letang (CREATIS CNRS-Engineering)

Radiation Effects
Mathilde Badoual (IJClab – IN2P3),
Michael Beuve (IP2I Lyon – IN2P3),
Patrick Vernet (LPCA-IN2P3), Lucie Sancey (IAB – CNRS Biology)

Radionucleides
Ferid haddad (SUBATECH-IN2P3 / GIP ARRONAX)
Ali Ouadi (IPHC – IN2P3)

Cross-cutting Themes

Biology
Lucie Sancey (IAB- CNRS Biology),
François Paris (Inserm)

Clinical Applications
Juliette Thariat (LPC-IN2P3/CHB Caen)

Computing
Lydia Maigne (LPCA – IN2P3), Jean-Michel Letang (CREATIS- CNRS Engineering)

Instrumentation
Mathieu Dupont (CPPM-IN2P3)

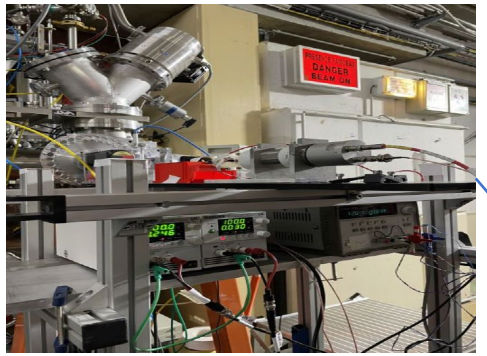
Irradiation Platform
Charbel Koumeir (GIP ARRONAX)

External Relations

SFPM	SFBR	Inserm
Ludovic Ferrer	Julie Costanzo	Jean-François Paris

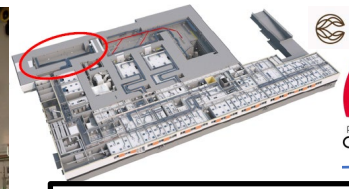
Irradiation platforms

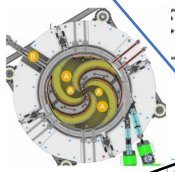
GANIL



ALTO

ARRONAX



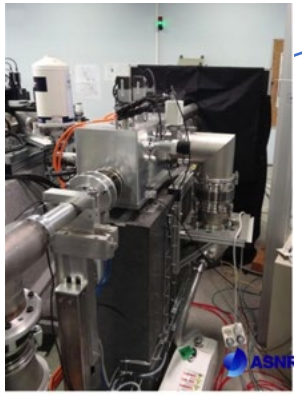


CYRCé

C400, carbon beams

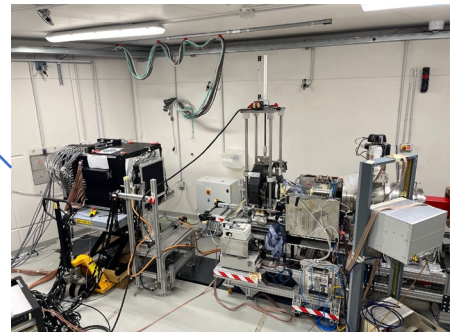
With dedicated « research rooms » = on-going discussion with IN2P3 and others partners!

AIFIRA



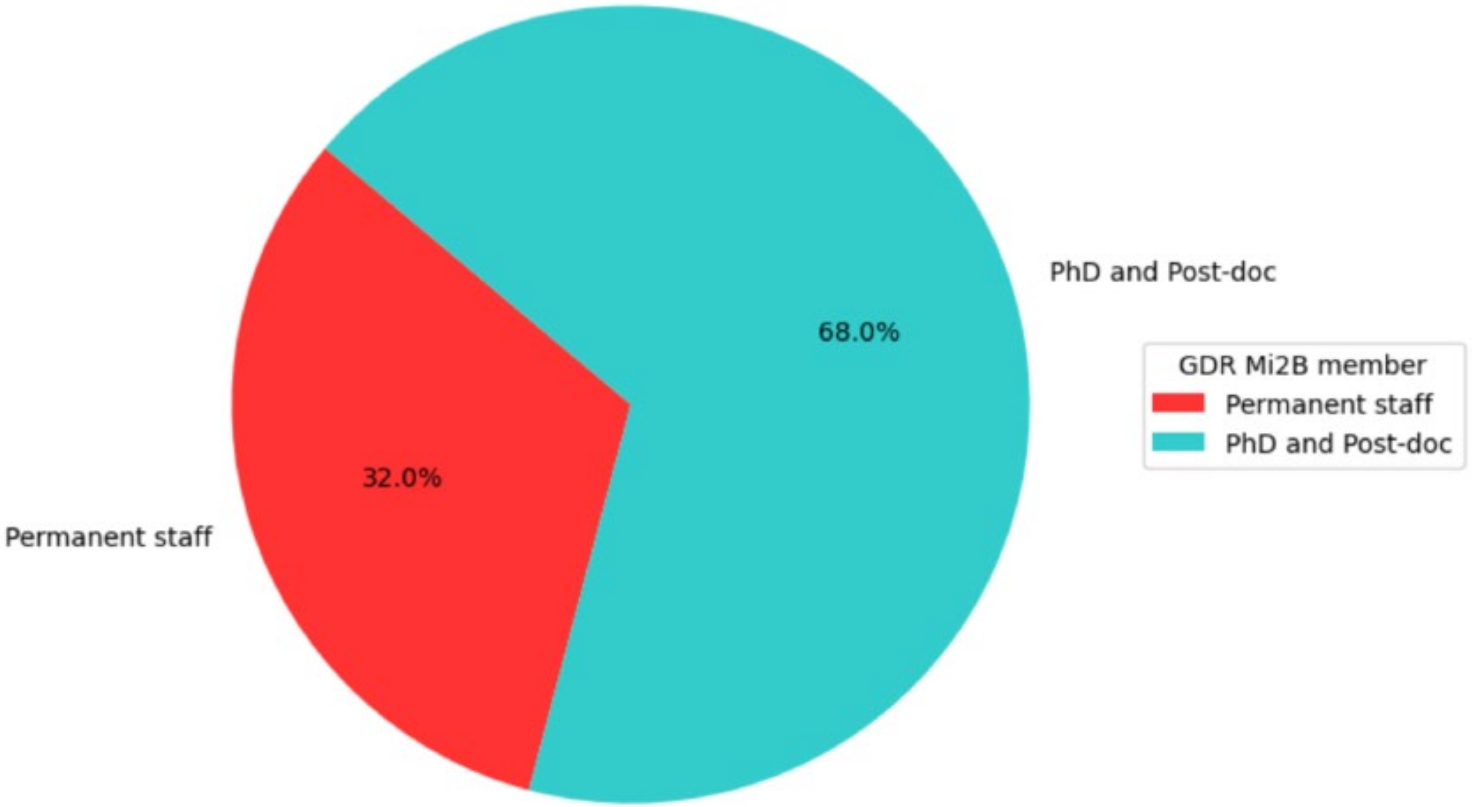
CAL, Nice

CNAO



GDR MI2B members

Predominant role played by non-permanent staff – mainly Young Scientists

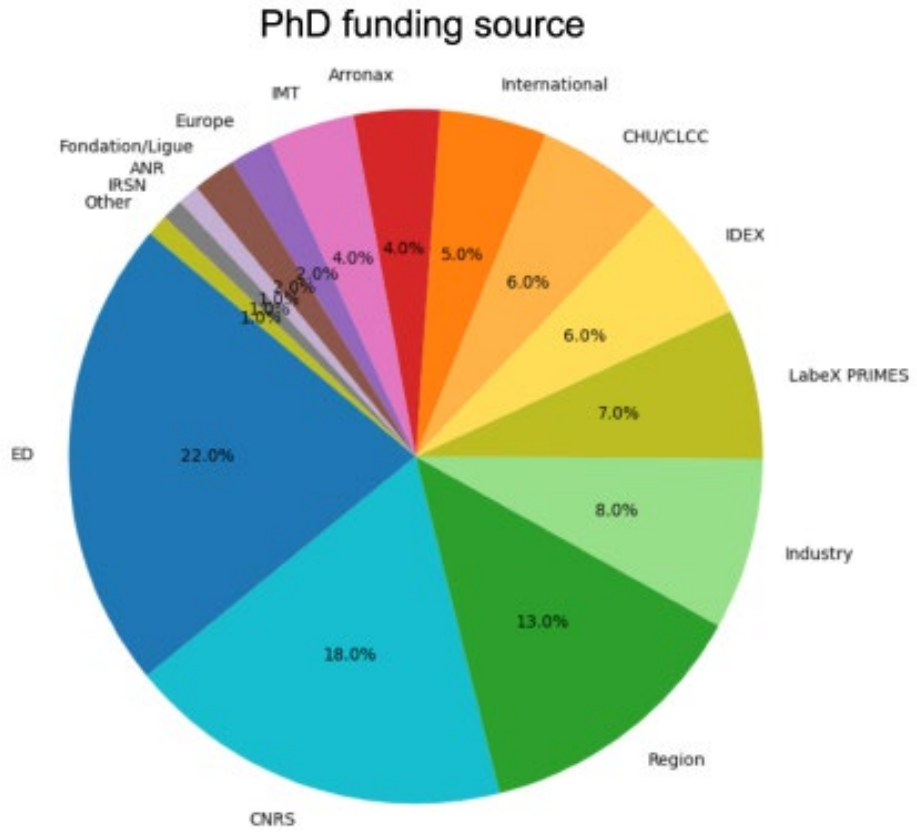


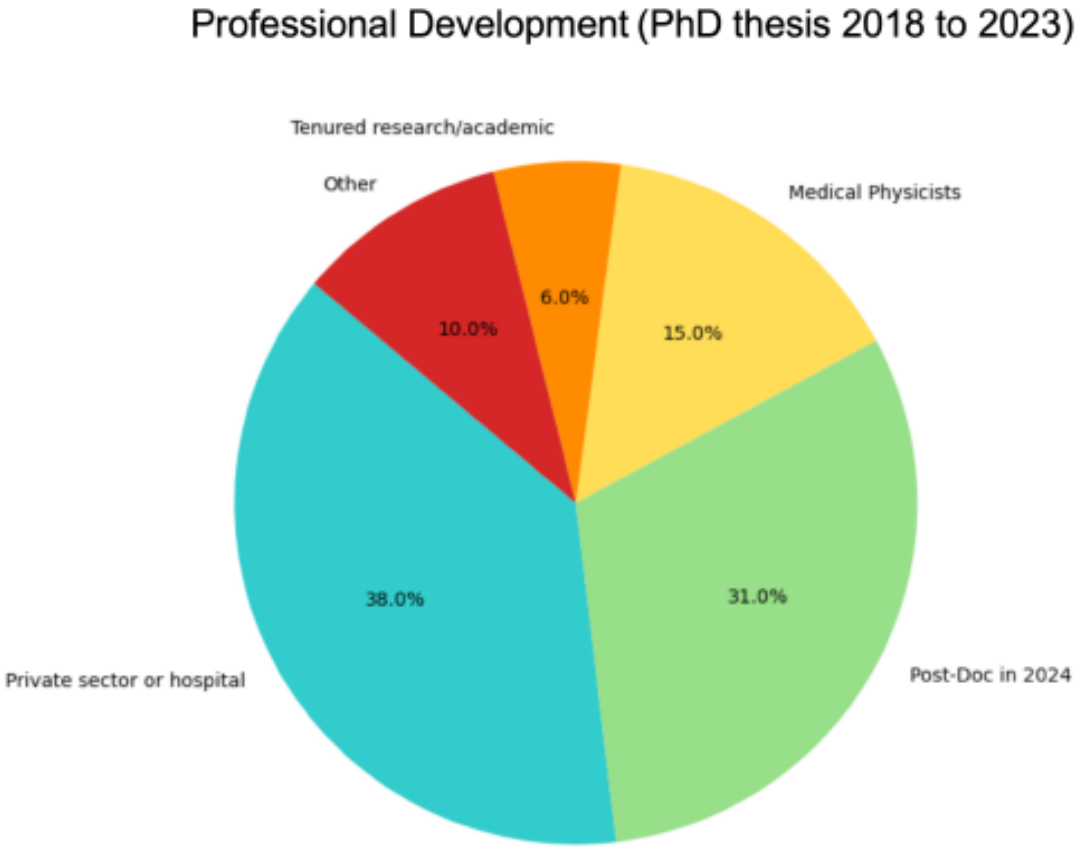
Role of GDR: education and training

- **Young researchers present at AGs** (oral/poster)
- **Thematic schools:**
  - **"Physics for Radiobiologists"** (Aussois 2024) is to be repeated every two years starting in 2026.
  - Alternating with a **similar initiative: "Radiobiology for Physicists",** inspired by the 2024 Joliot-Curie school in Oléron (potential partners: RADIOTRANSNET, SFBR, …).

Young Scientists

Results of a survey conducted in 2024 through the GDR MI2B among all its members.





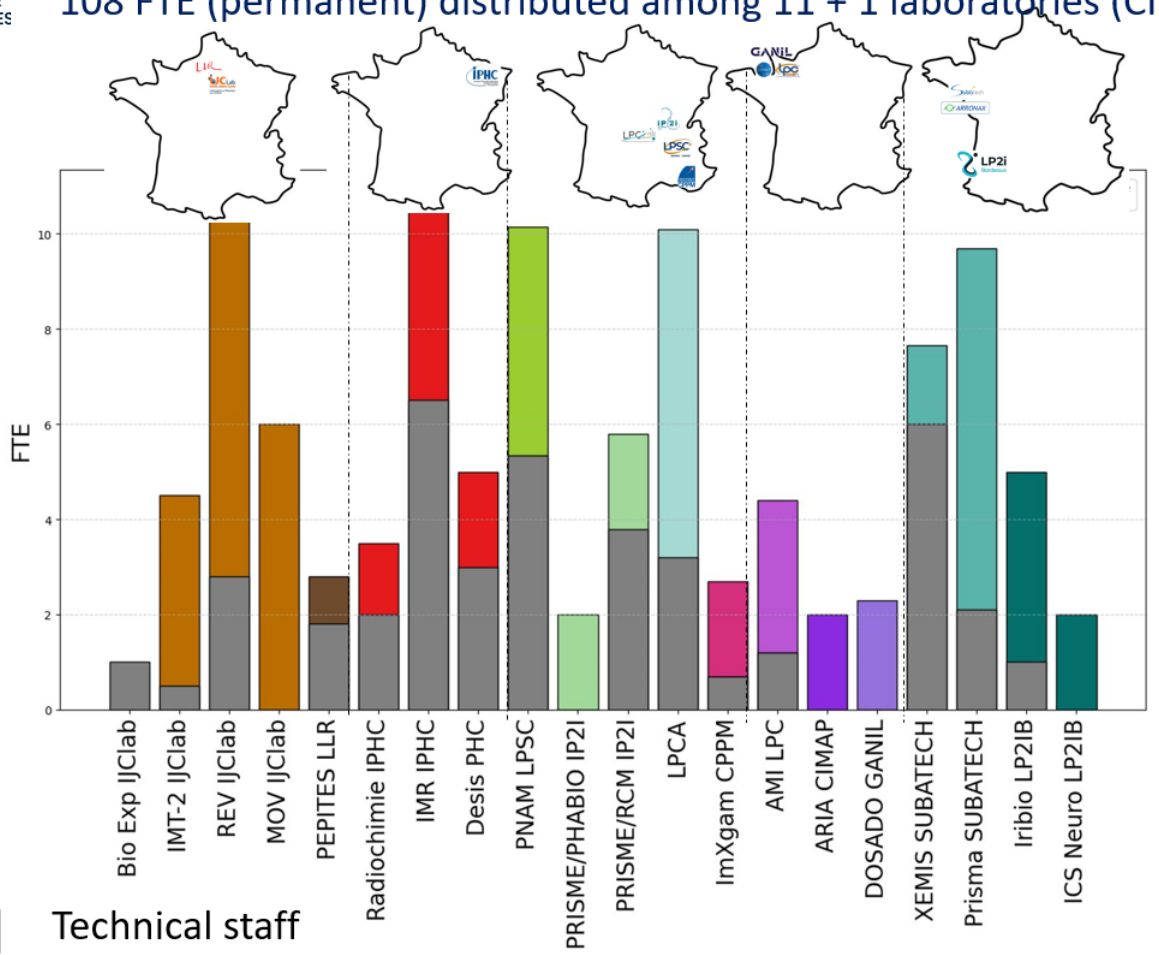
We can be glad that our PhD students find professional opportunities and are not left behind, **but the proportion of them who go on to renew our workforce remains sadly too low to ensure the long-term sustainability of our teams**

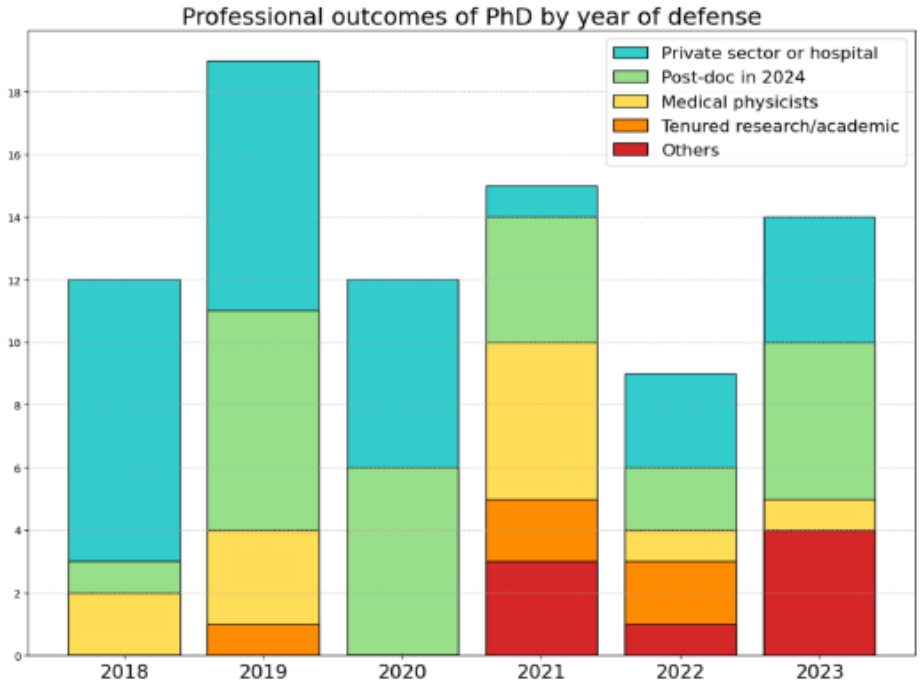
What about the future ?

NUCLÉAIRE & PARTICULES

2025

~108 FTE (permanent) distributed among 11 + 1 laboratories (CIMAP)

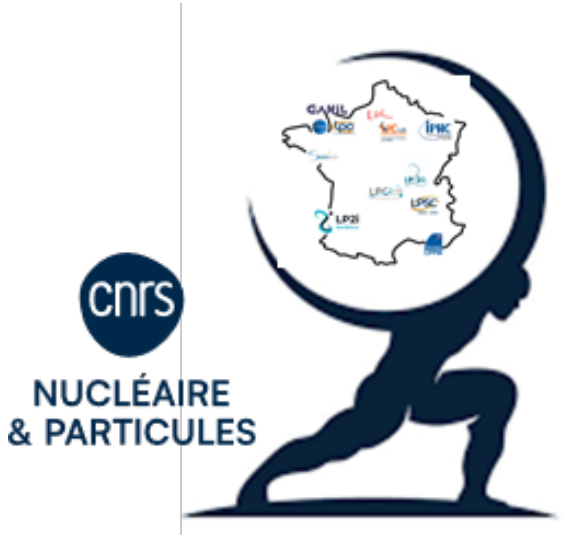




Tenured research / academic

5 years perspectives

Towards a new organization in 4 Master Projects



New in 2025

Status of therapeutic approaches

- **External therapies using different ion types in hadron therapy**: protons, helium, carbon, ...
- **External therapies** (e.g., X-rays or hadron therapy**) with spatial** (micro- or mini-beams) **and/or temporal fragmentation** (FLASH).
- **Internal radiotherapy within the theranostic approach**
- **Combined external** (X-ray or hadron therapy) **and internal therapies** (e.g. radionuclide therapy, BNCT...).

With the following scientific objectives:

- **Significantly improving the effectiveness of treatments** for cancers that are **radioresistant**, **recurrent**, **therapeutically unresponsive**, **metastatic or diffuse** by combining particles with low and high LET.
- **Enabling dose hypofractionation** to achieve effective tumor volume reduction while minimizing damage to surrounding healthy tissues => **improving treatment tolerance for patients.**
- Moving toward personalized medical practices through **theranostic approaches** that combine therapy and diagnostics

Towards a new organization in Master Project

Hadrontherapy

FLASH

Targeted Radiotherapies

Radionuclides for therapy and diagnosis

Towards a new organization in Master Project

Hadrontherapy	FLASH	Targeted Radiotherapies	Radionuclides for therapy and diagnosis
WP			
WP			
WP			
WP			

With a matrix structure thanks to the definition of a serie of Work Packages (WP) specific to each MP but based on our reconized expertise in :

- **modeling,**
- **imaging,**
- **instrumentation,**

….

With 5 Years objectives and delivrables (currently under discussion)

Towards a new organization in Master Project

Hadrontherapy

FTE = 15,3 Researchers
19,6 Technical staff

FLASH

FTE = 6,3 Researchers
7,2 Technical staff

Targeted Radiotherapies

FTE = 10,3 Researchers
11,4 Technical staff

Radionuclides for therapy and diagnosis

FTE = 15,5 Researchers
10,1 Technical staff

Conclusion 1/2

- This talk was aimed to give you a broad **landscape of Health-related research at IN2P3**

…. Focussing:

- **interdisciplinary developments** in radiation physics, imaging, radiobiology, and radiotherapy.

…. Highlighted:

- **the structuring role of the GDR MI2B** in coordinating these activities

…. Fostering:

- local, national and international **collaborations**

… Outlining:

- **new organizational perspectives within IN2P3** with the construction of **Master Projects (started in March 2025)**

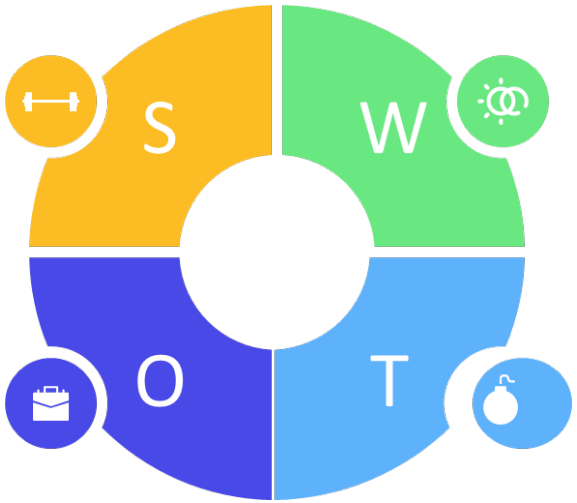
CONCLUSION 2/2

Strengths

- **Highly interdisciplinary** projects
- **Unique set** of **irradiation platforms**
- **Access to clinical facilities** (CNAO, CAL)
- **Strong partnerships** (CNAO, INFN, GSI, GANIL…)
- **High succes** with **funding agencies**
- **Expertise in instrumentation and modeling** (leadership in highly-used open-source code)
- **Strong links with Inserm, CHU and Cancer centers**

Opportunities

- **Collaborative works** with many national institutions (INSERM, CNES, clinical facilities) and regional structures
- **Possible transfer to industry or clinical routine** (e.g., online monitoring)
- **Commissioning of the C-400**
- **New accelerators techniques** (e.g. laser)



Weaknesses

- Difficulty **securing external funding for long-term projects**
- **Human Resources**
- **Dependence on external irradiation facilities**
- **High dependence on radionuclide availability slowing-down TRT research**

Threats

- **Strong competition for fundings**
- **Risk of project slow-down due to staff turnover or lack of recruitment**
- Constraints associated with international **beam time access**
- **Uncertainty in long-term institutional or political support for interdisciplinary research**
- **Lack of attractiveness due to low amount of permanent academ positions**
- **Cost of access to clinical beam**

cnrs GDR Groupement de recherche

MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

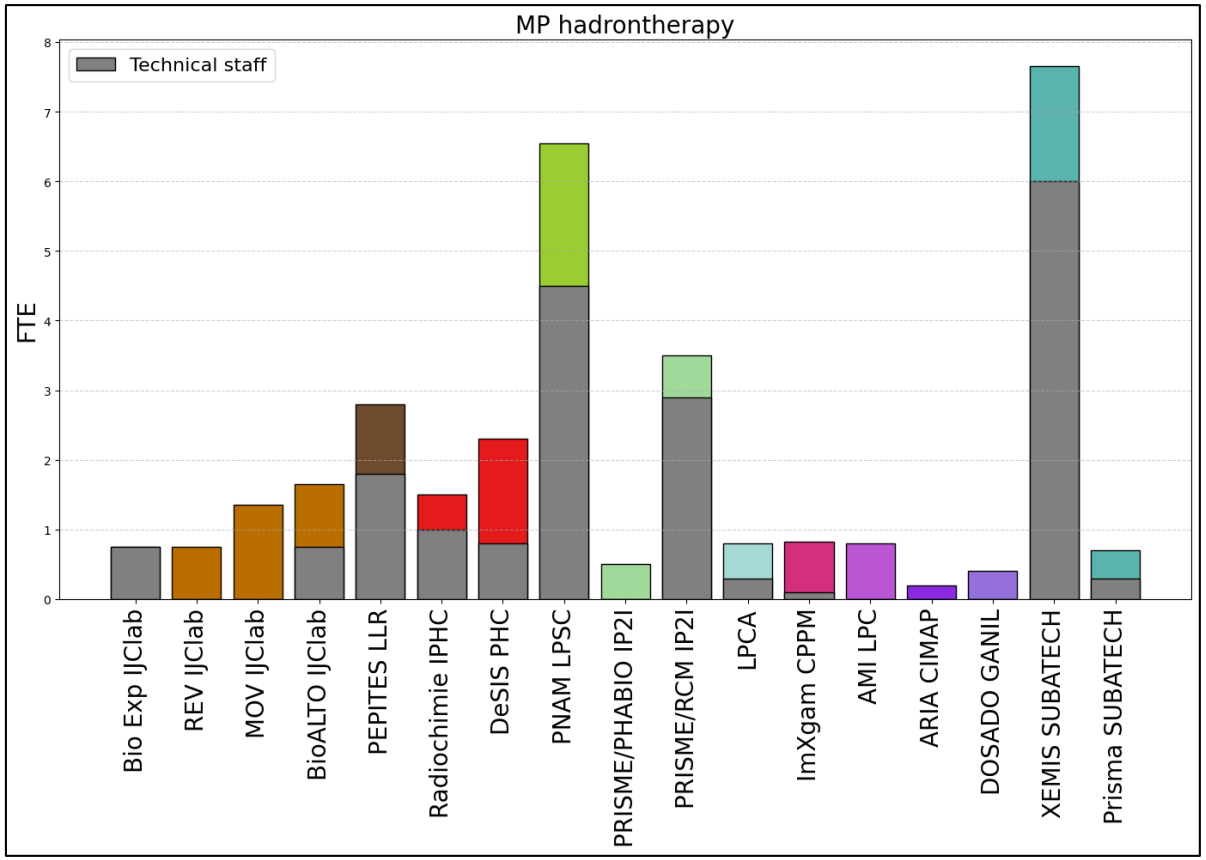
Thanks for your attention

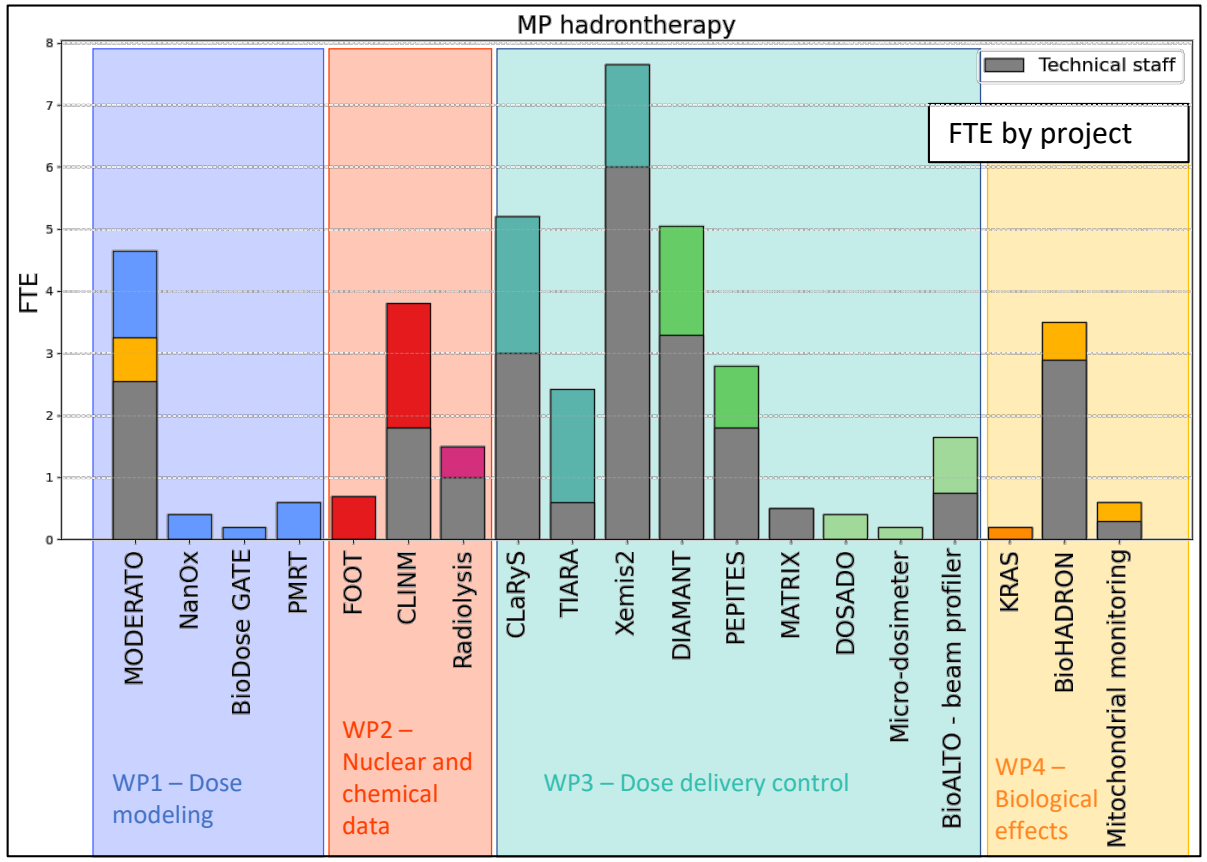
cnrs GDR Groupement de recherche

MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

Back-up

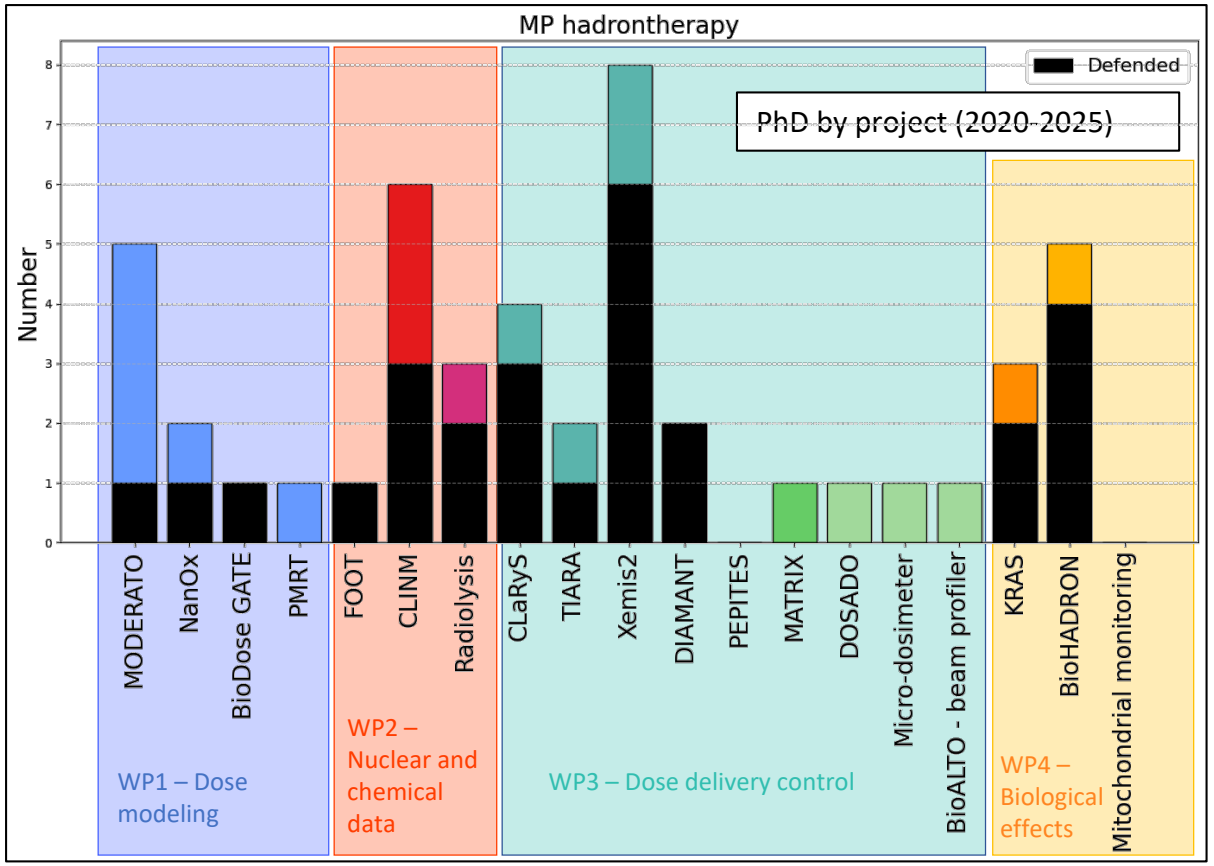
FTE in the Hadrontherapy Master-project of **in2p3**



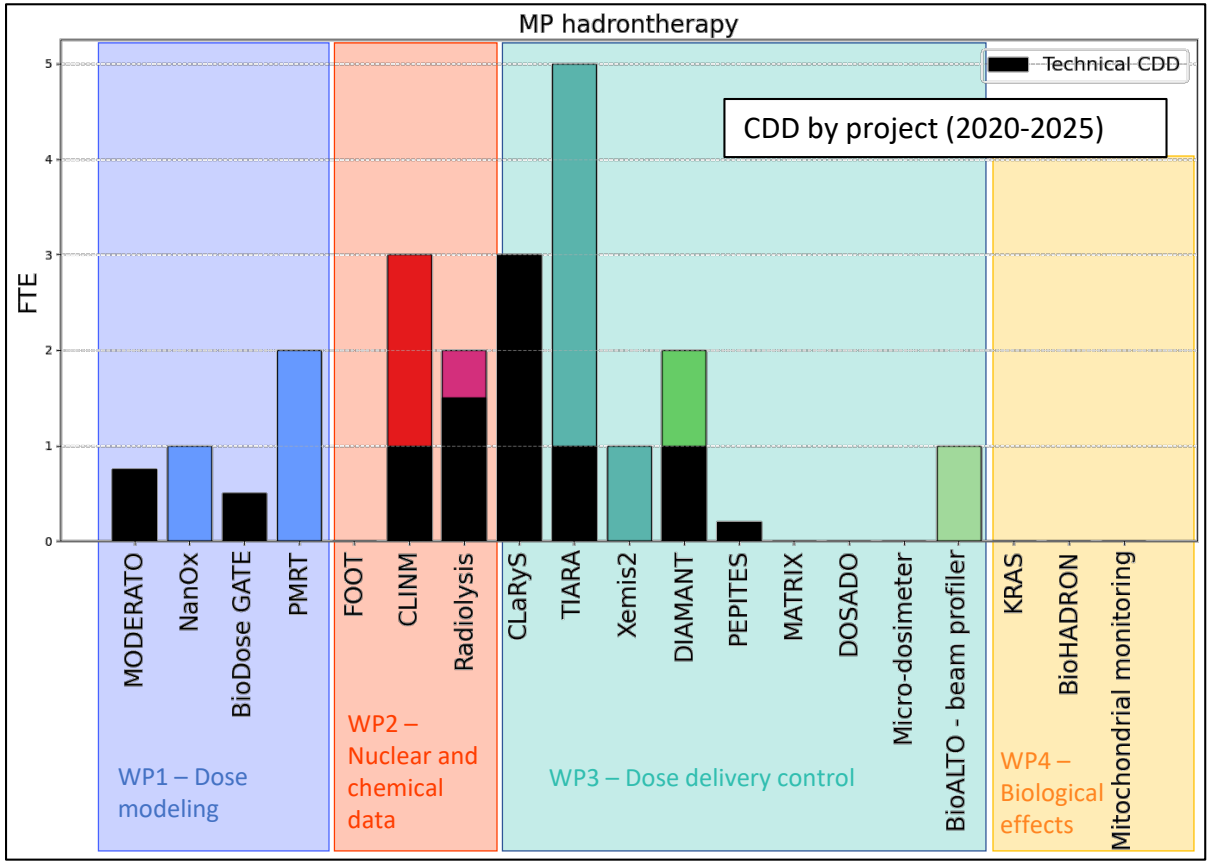


Total FTE in Hadrontherapy MP: 15.33 researchers, 19.60 technical staff

FTE in the Hadrontherapy Master-project of **in2p3**

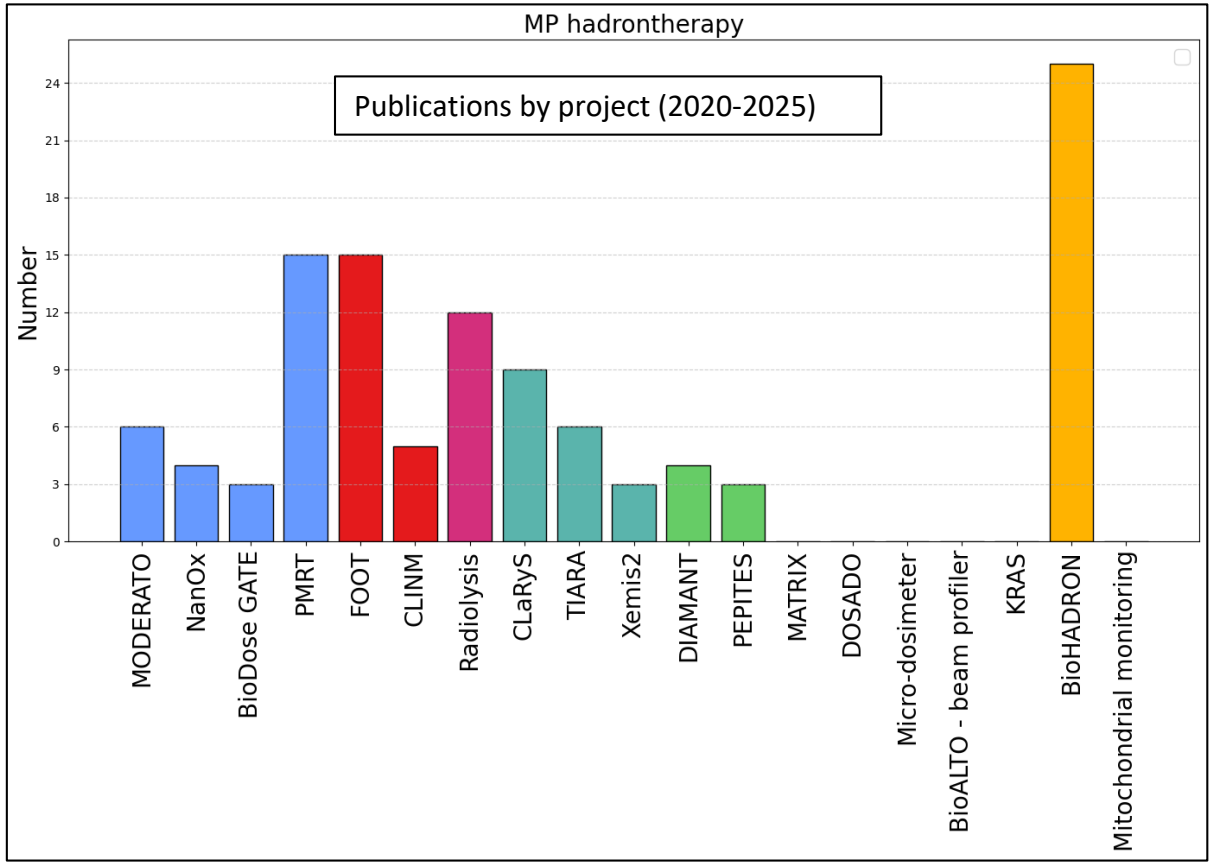


Total PhD in Hadrontherapy MP: 27 defended, 20 on-going

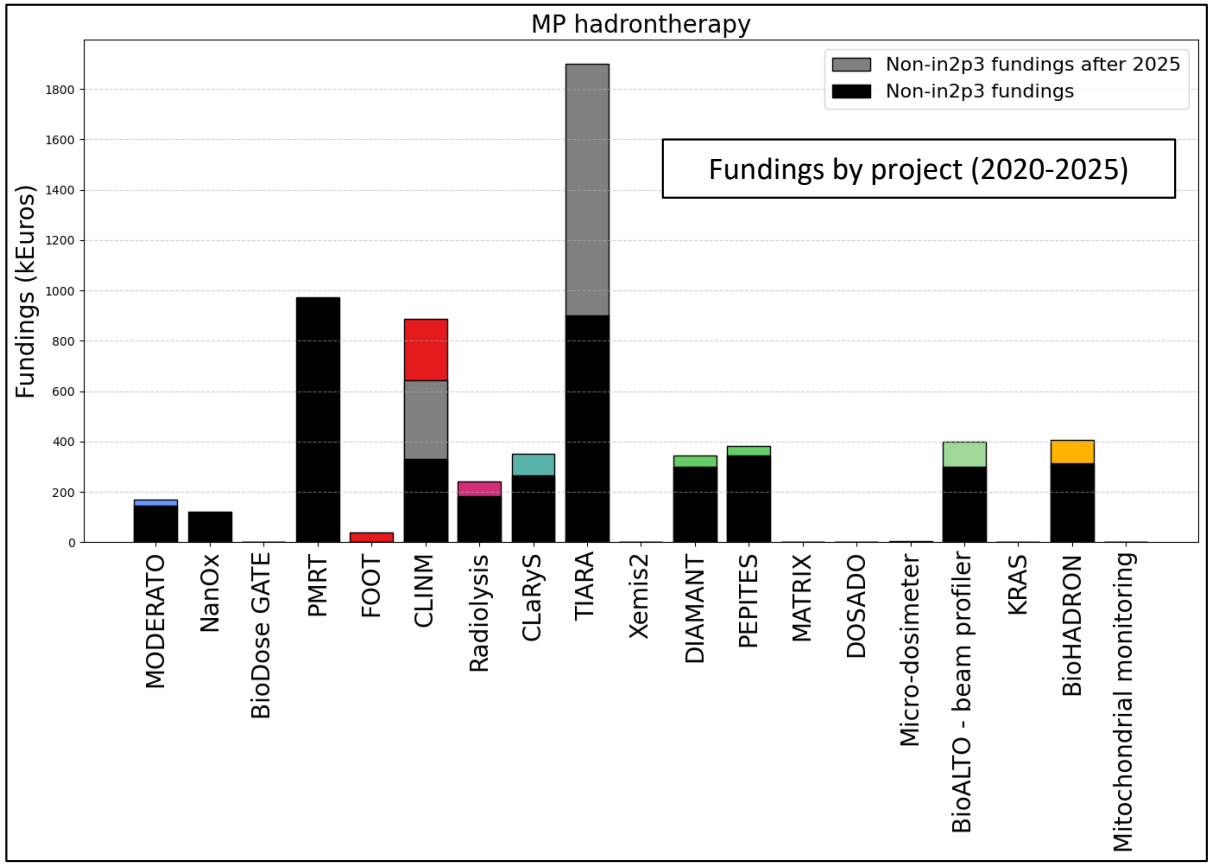


Total CDD in Hadrontherapy MP: 11.20 FTE researchers, 9 FTE technical staff

Publications & fundings in the Hadrontherapy Master-project of **in2p3**

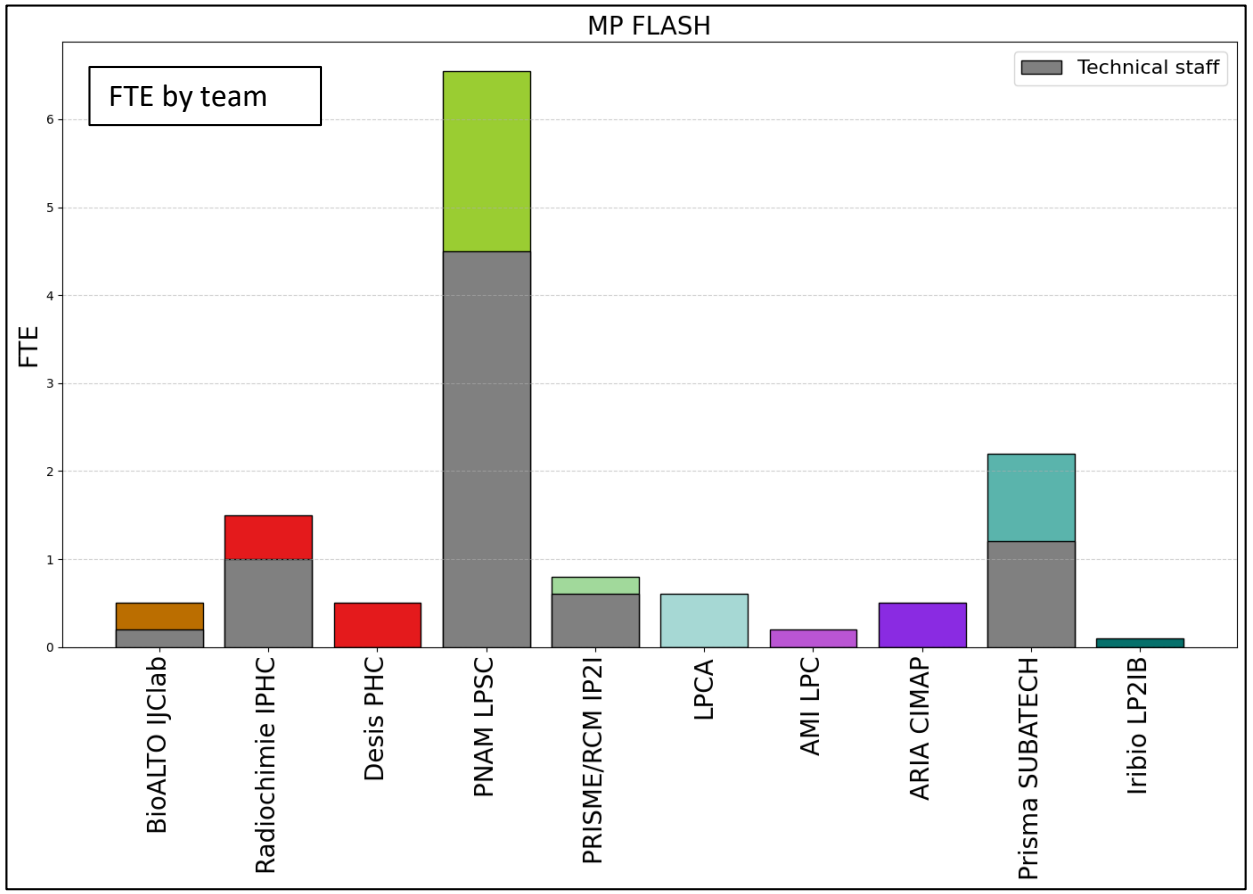


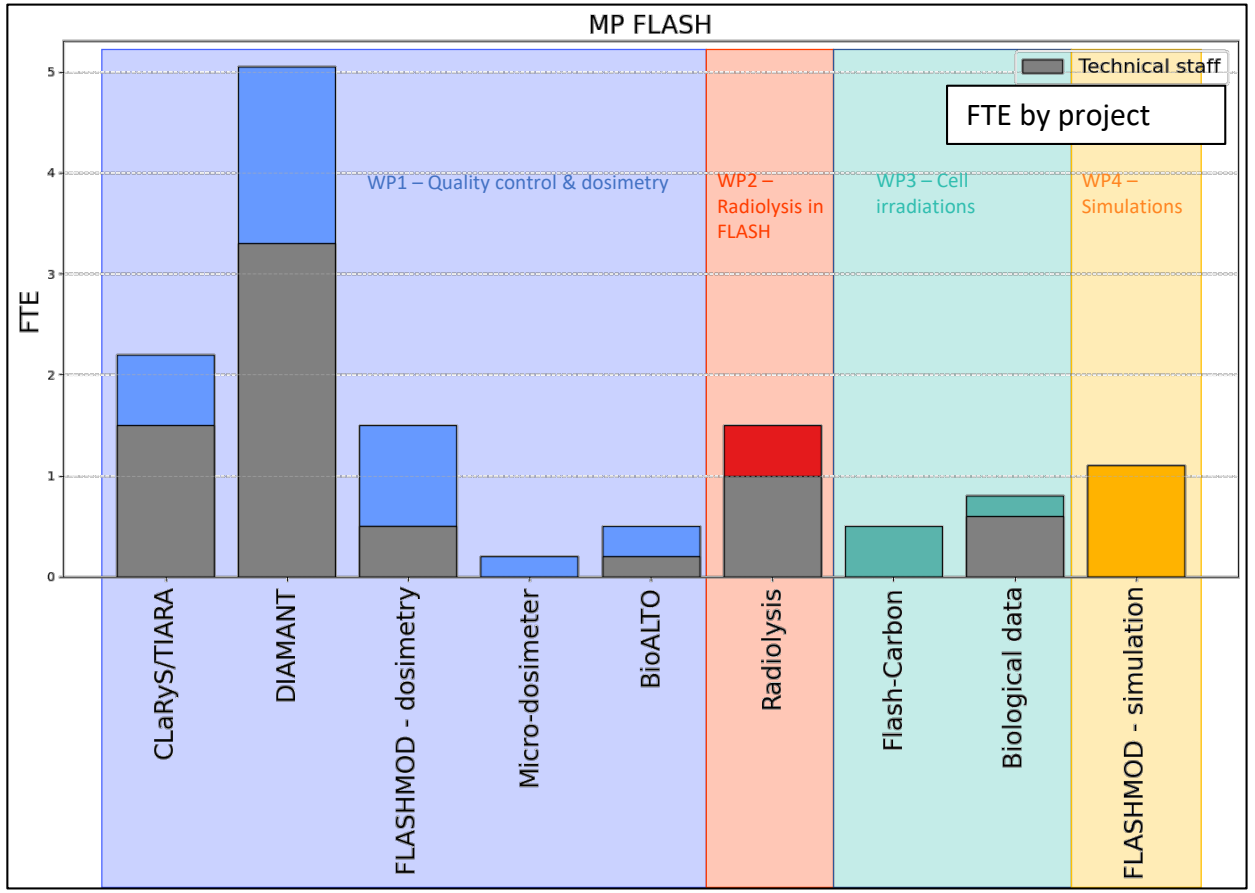
Total publications in Hadrontherapy MP: 111



Total fundings in Hadrontherapy MP: 1039 kEuros in2p3, 4058 kEuros non-in2p3

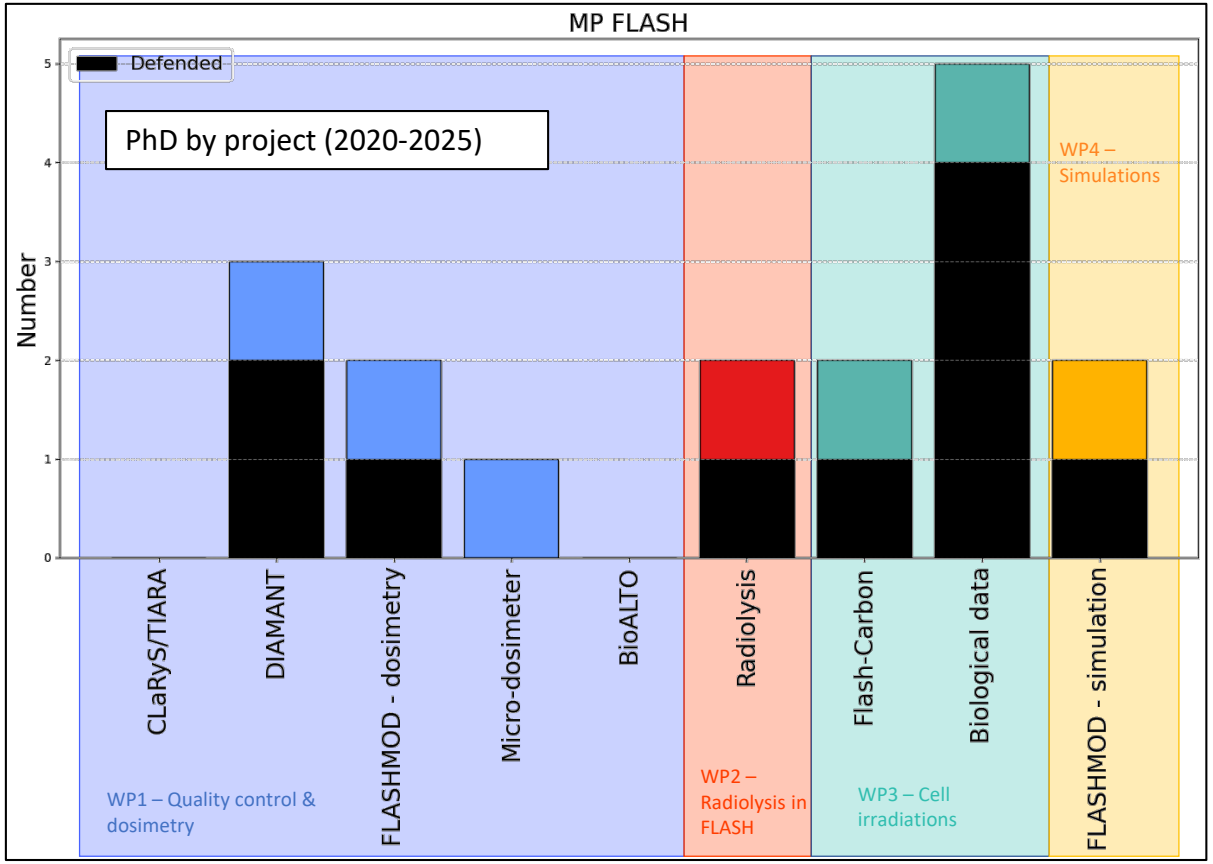
FTE in the FLASH Master-project of **in2p3**



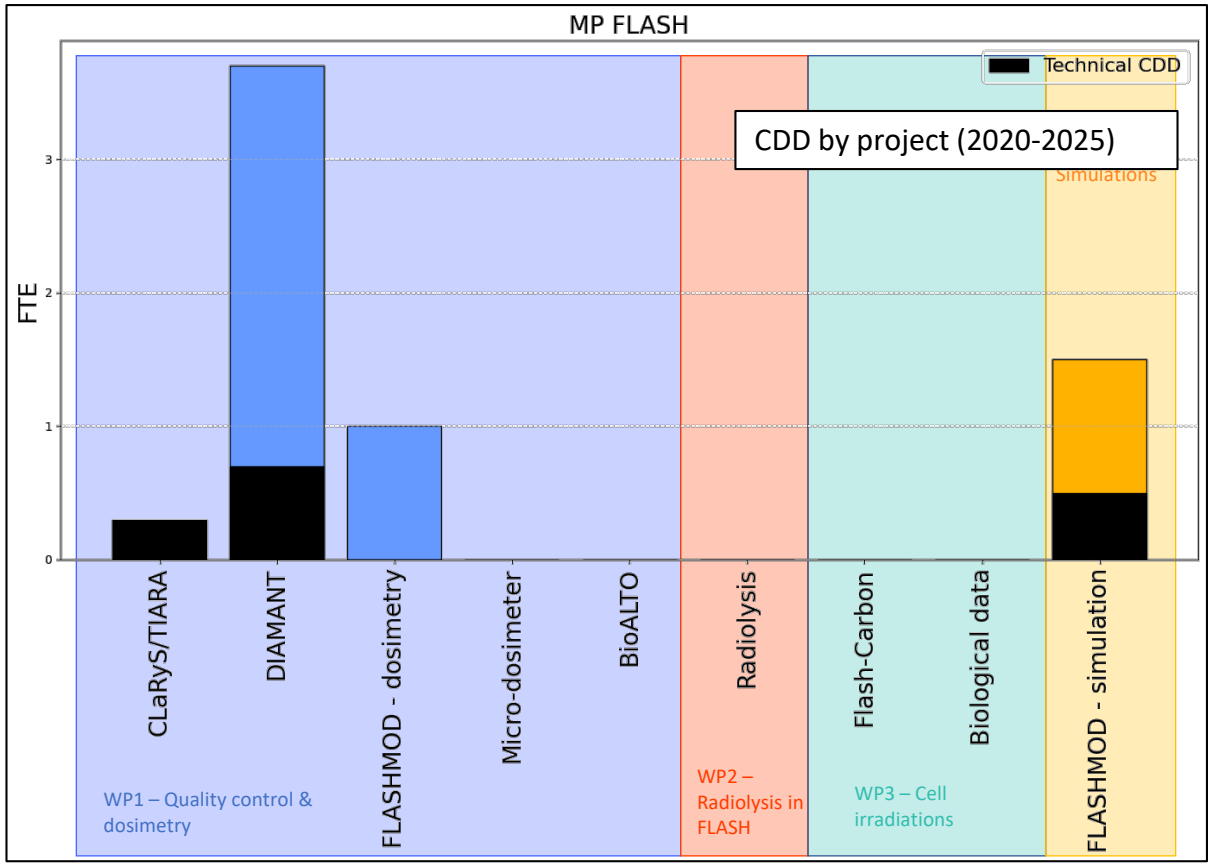


Total FTE in FLASH MP: 6.25 researchers, 7.20 technical staff

FTE in the FLASH Master-project of **in2p3**

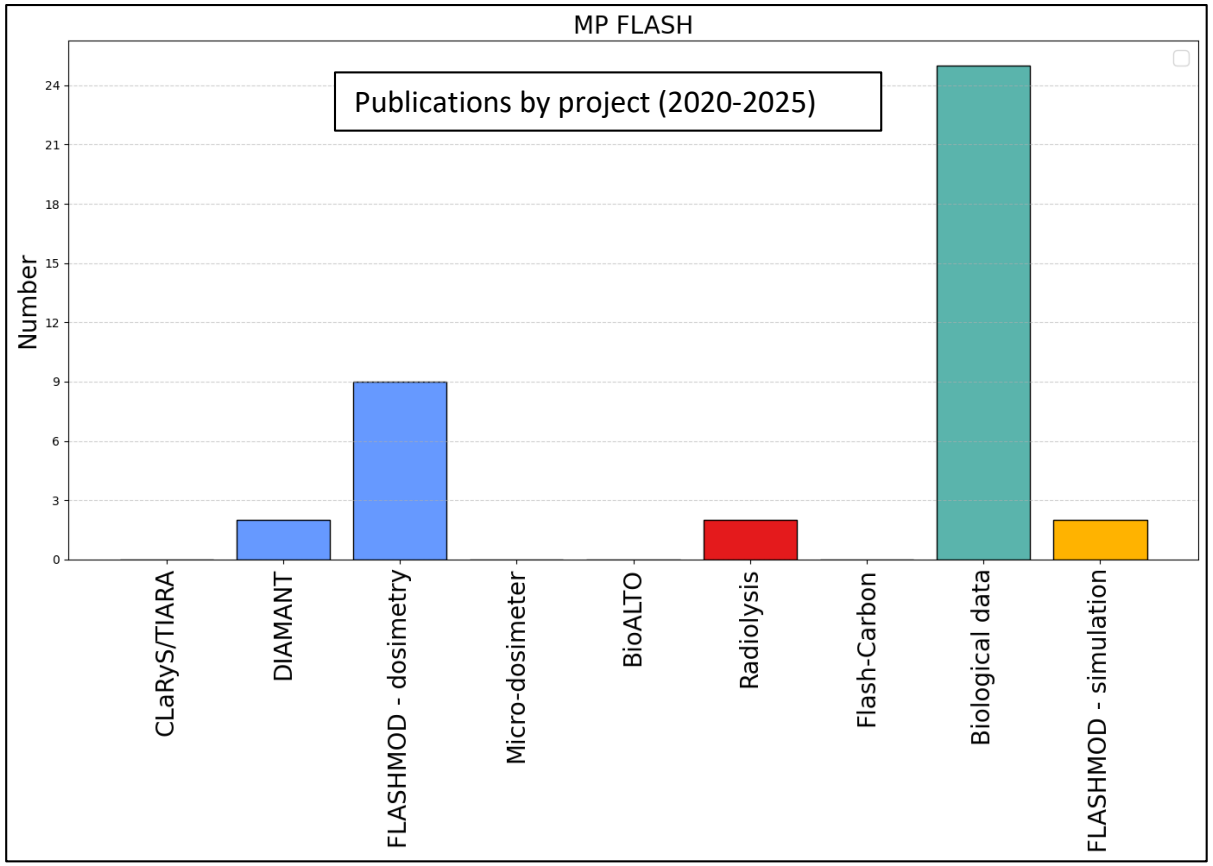


Total PhD in FLASH MP: 10 defended, 7 on-going

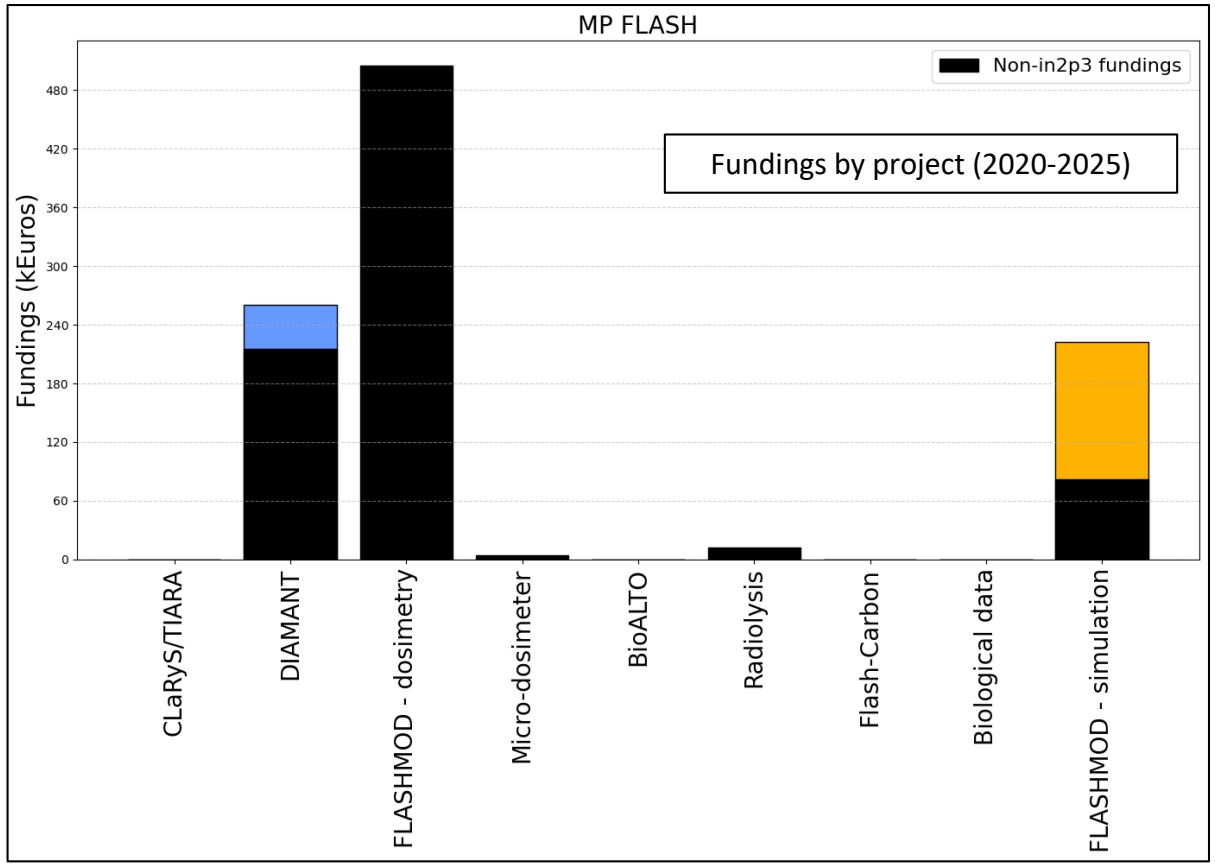


Total CDD in FLASH MP: 5 FTE researchers, 1.5 FTE technical staff

Publications & fundings in the FLASH Master-project of **in2p3**

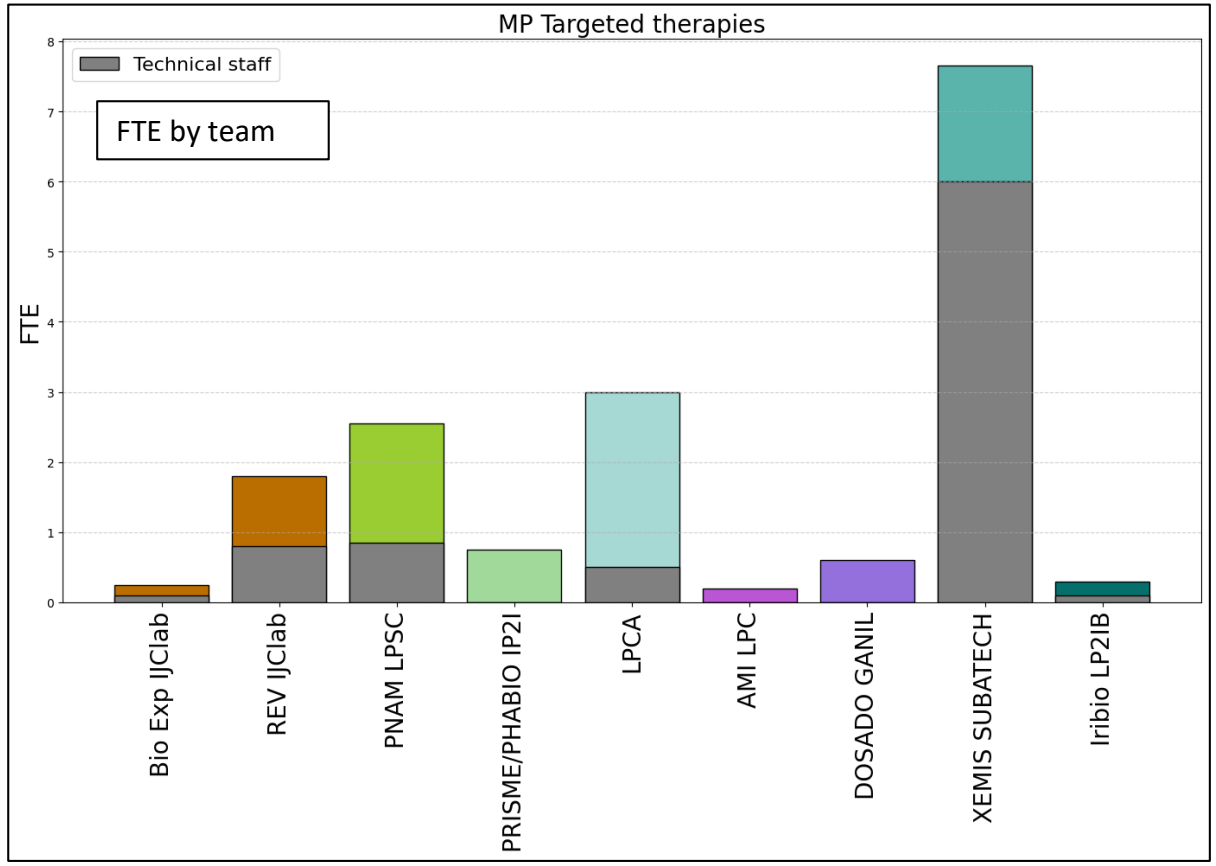


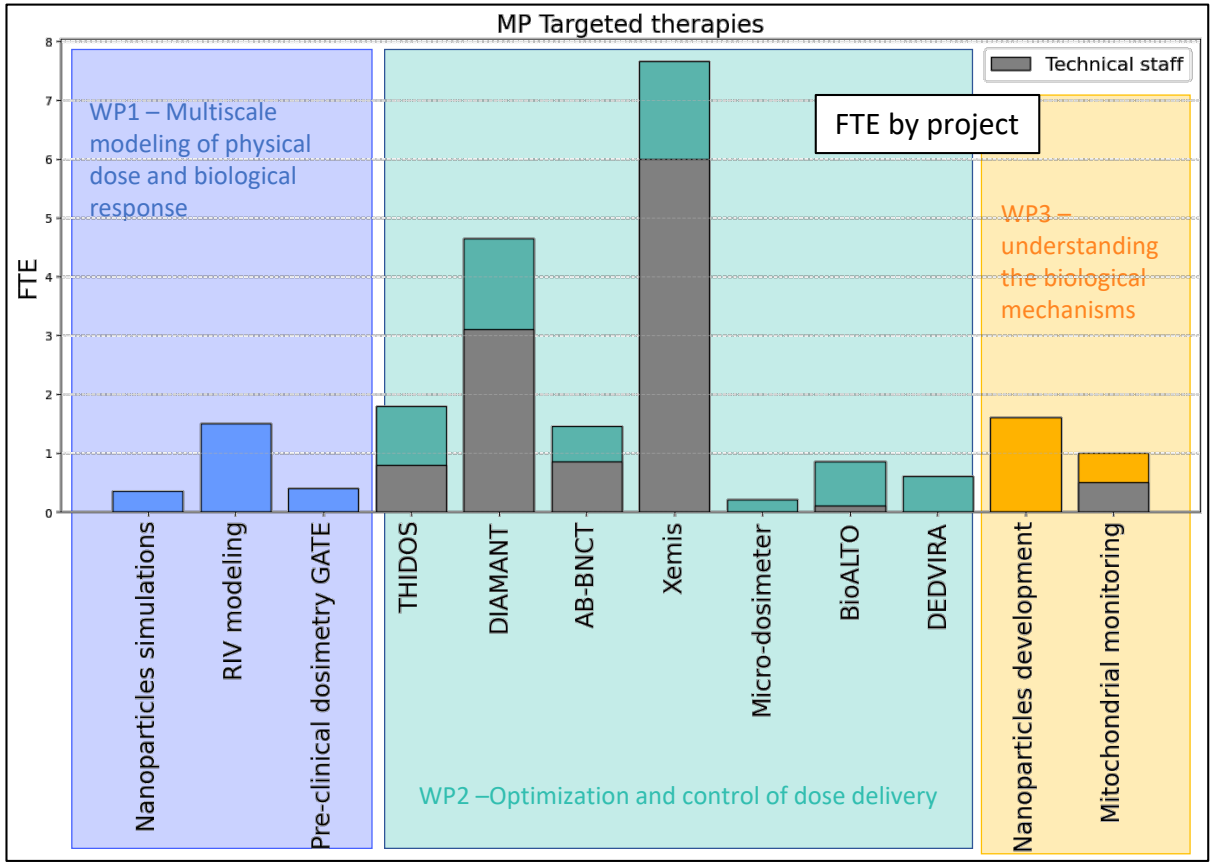
Total publications in FLASH MP: 40



Total fundings in FLASH MP: 185 kEuros in2p3, 818 kEuros non-in2p3

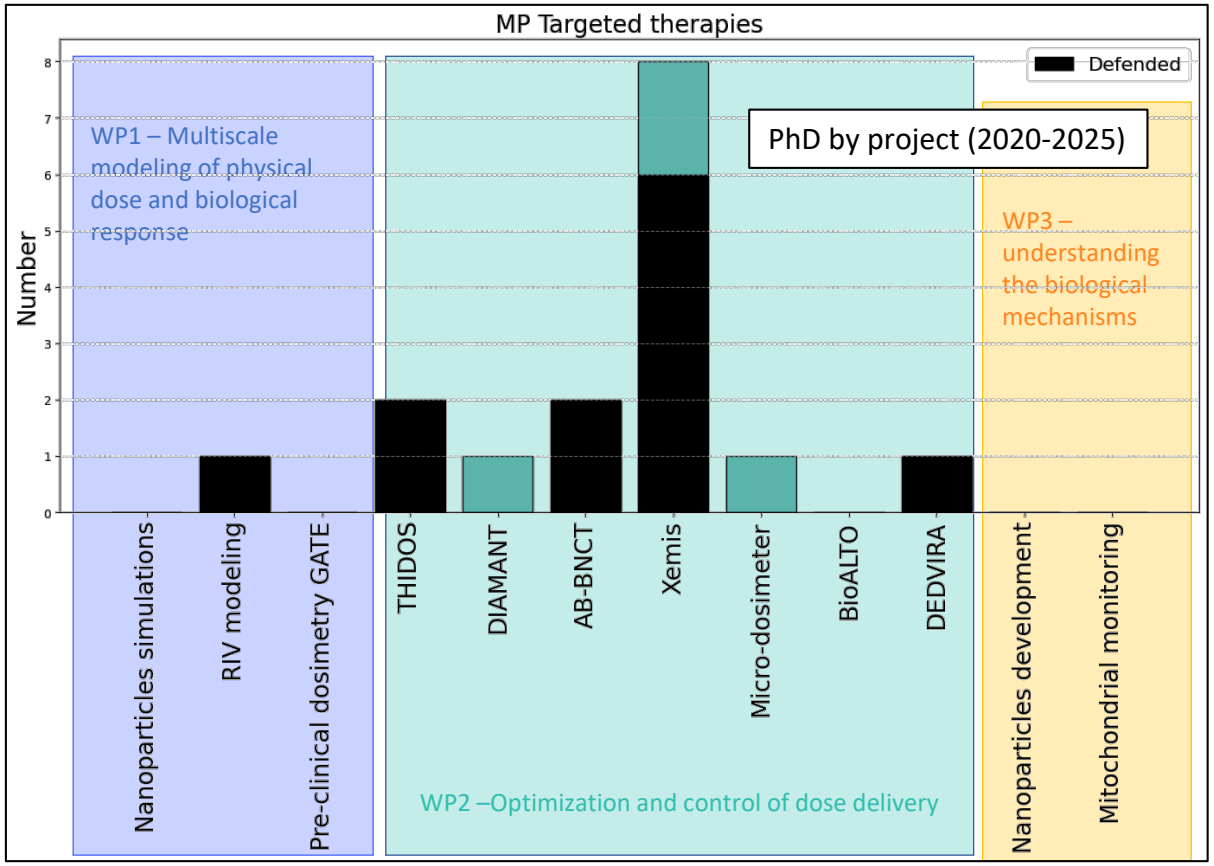
FTE in the targeted therapies Master-project of **in2p3**



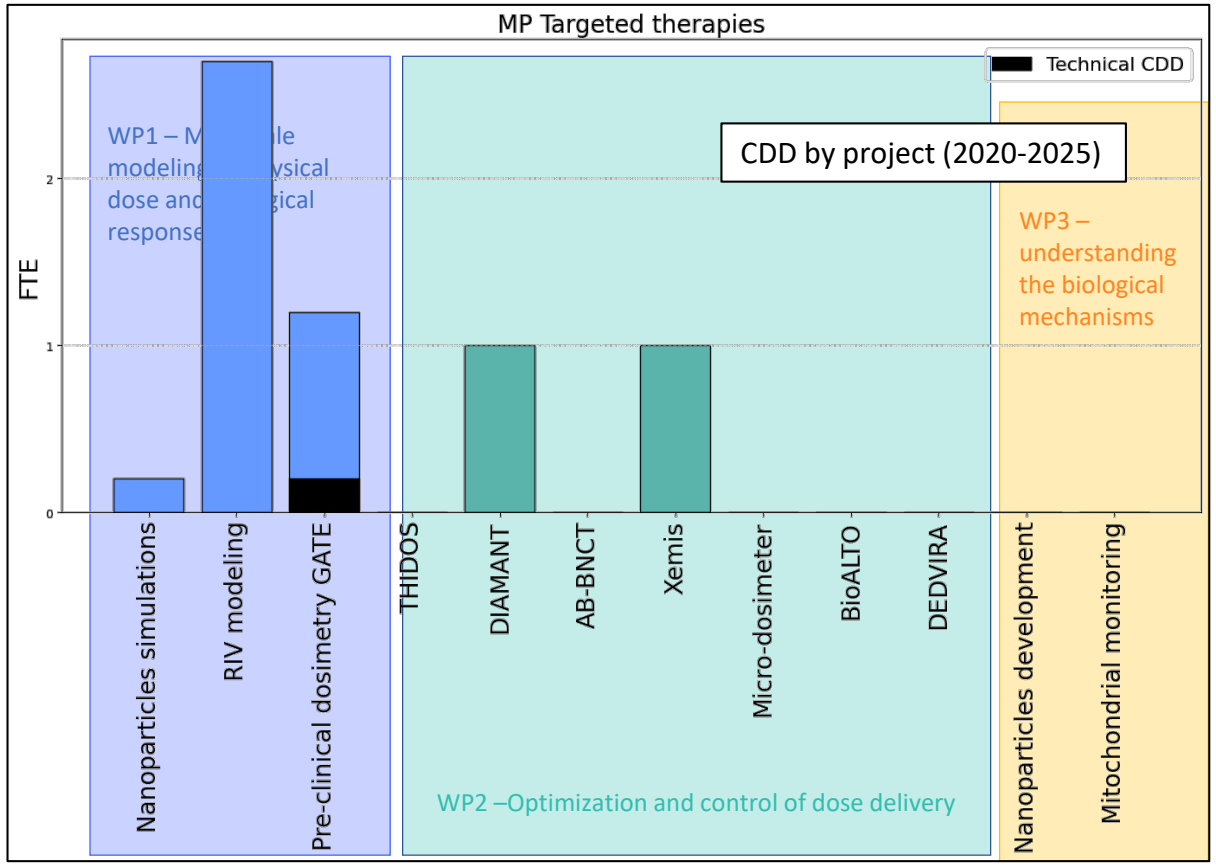


Total FTE in targeted therapies MP: 10.3 researchers, 11.35 technical staff

FTE in the targeted therapies Master-project of **in2p3**

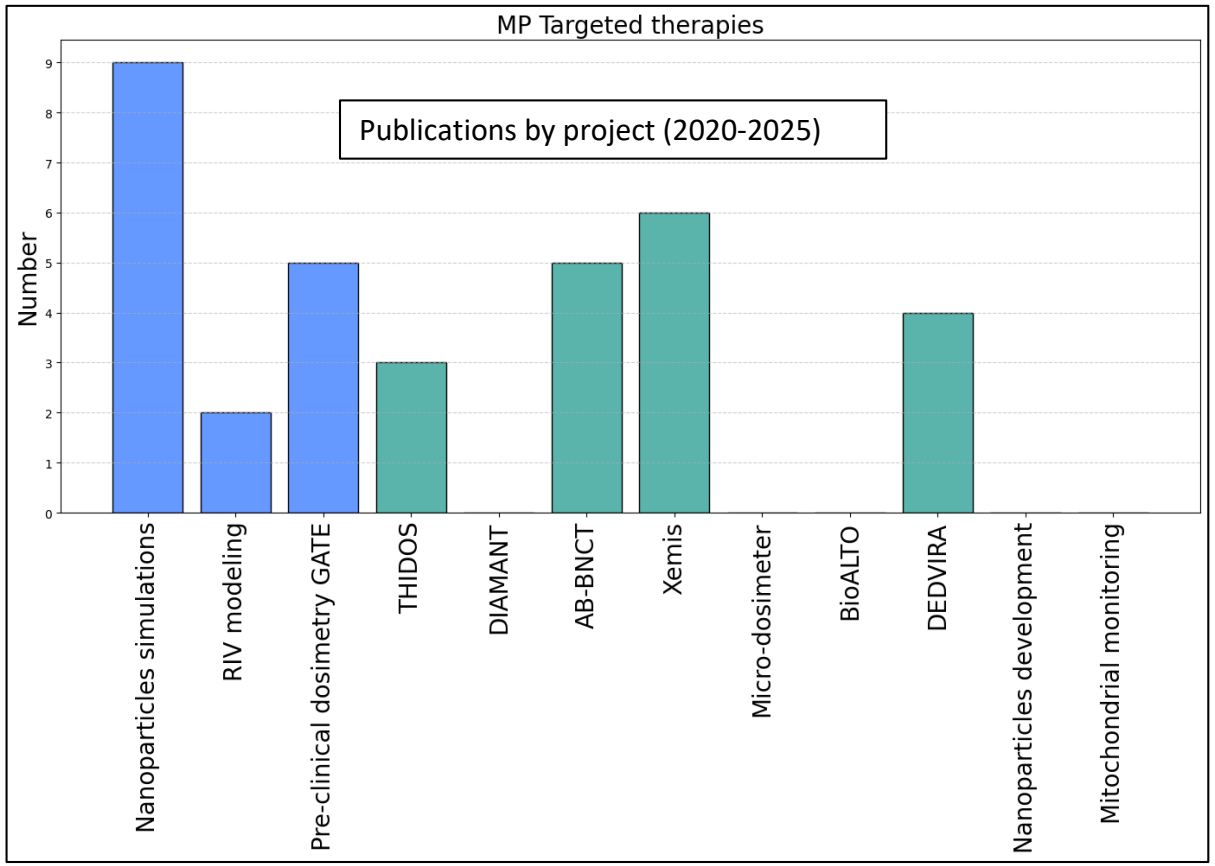


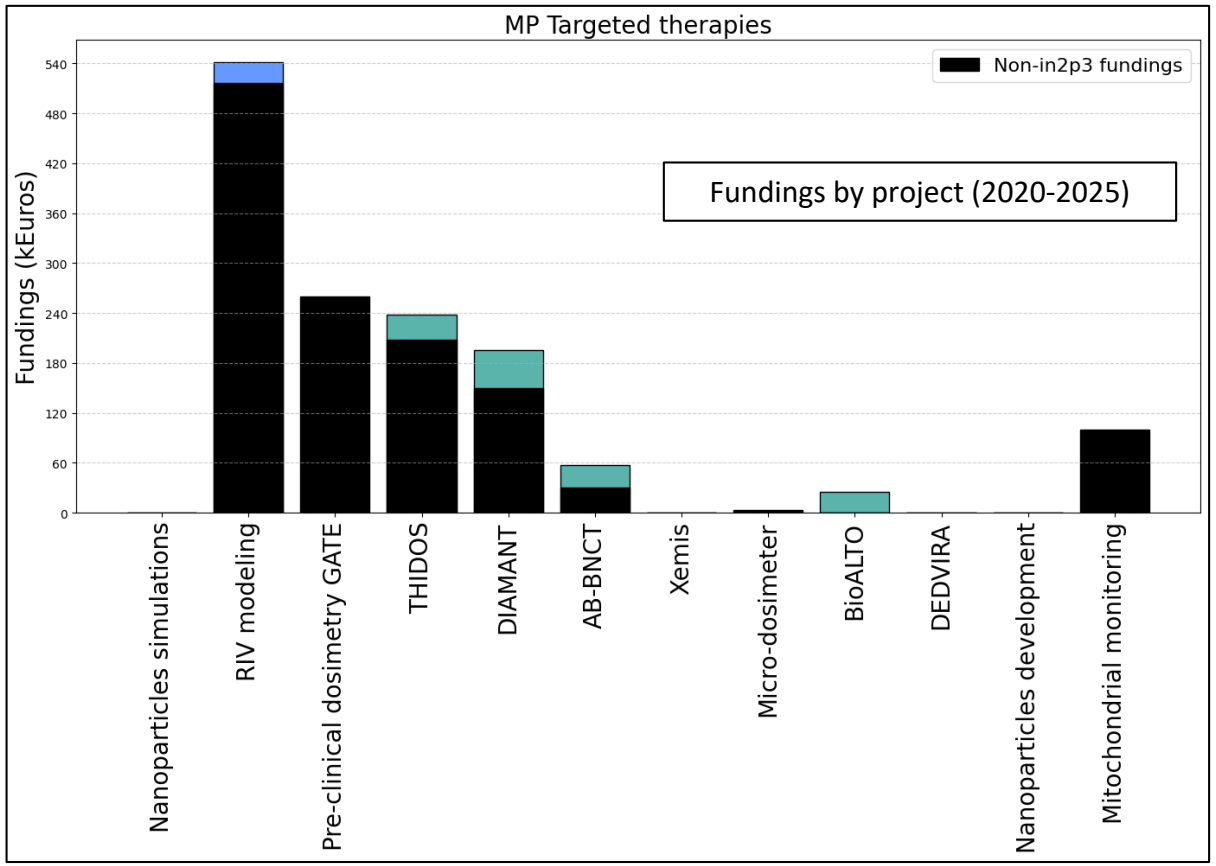
Total PhD in Targeted therapies MP: 12 defended, 4 on-going



Total CDD in Targeted therapies MP: 5.7 FTE researchers, 0.2 FTE technical staff

Publications & fundings in the targeted therapies
Master-project of **in2p3**

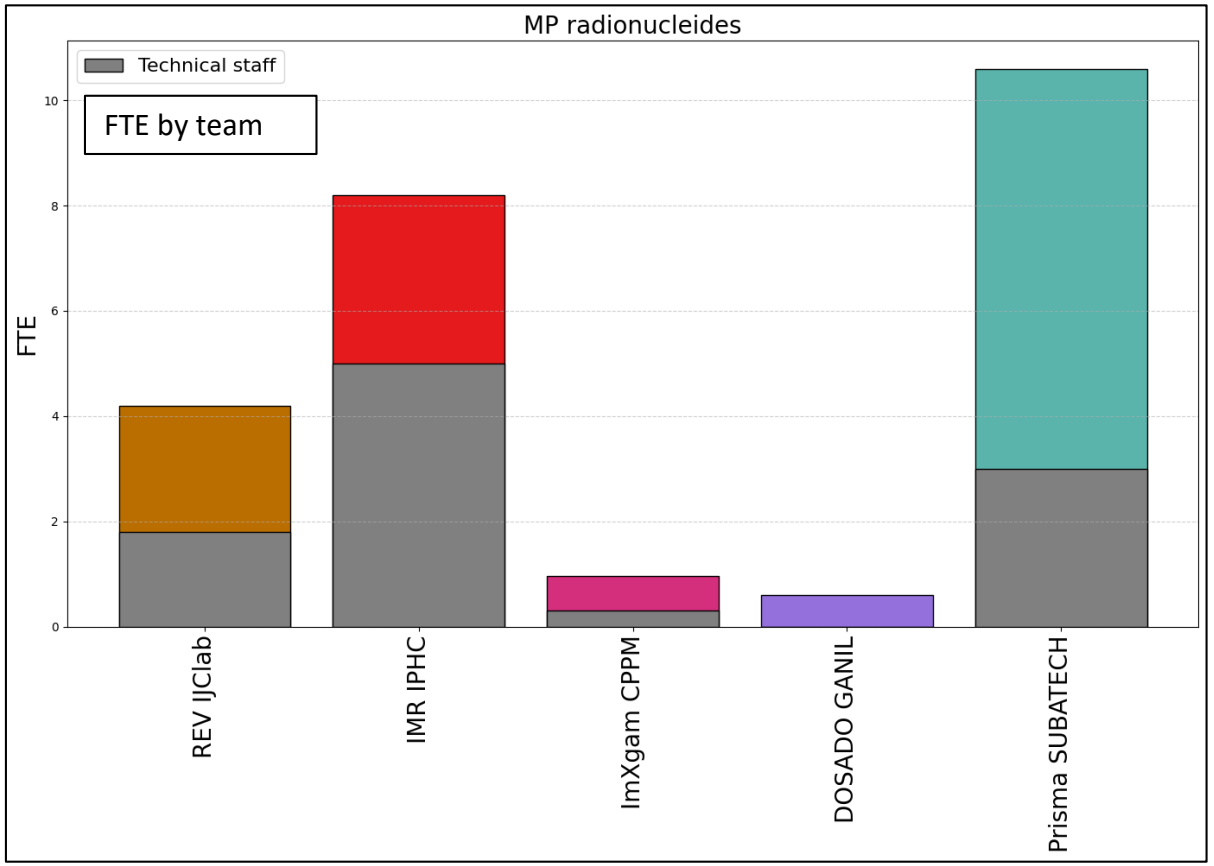


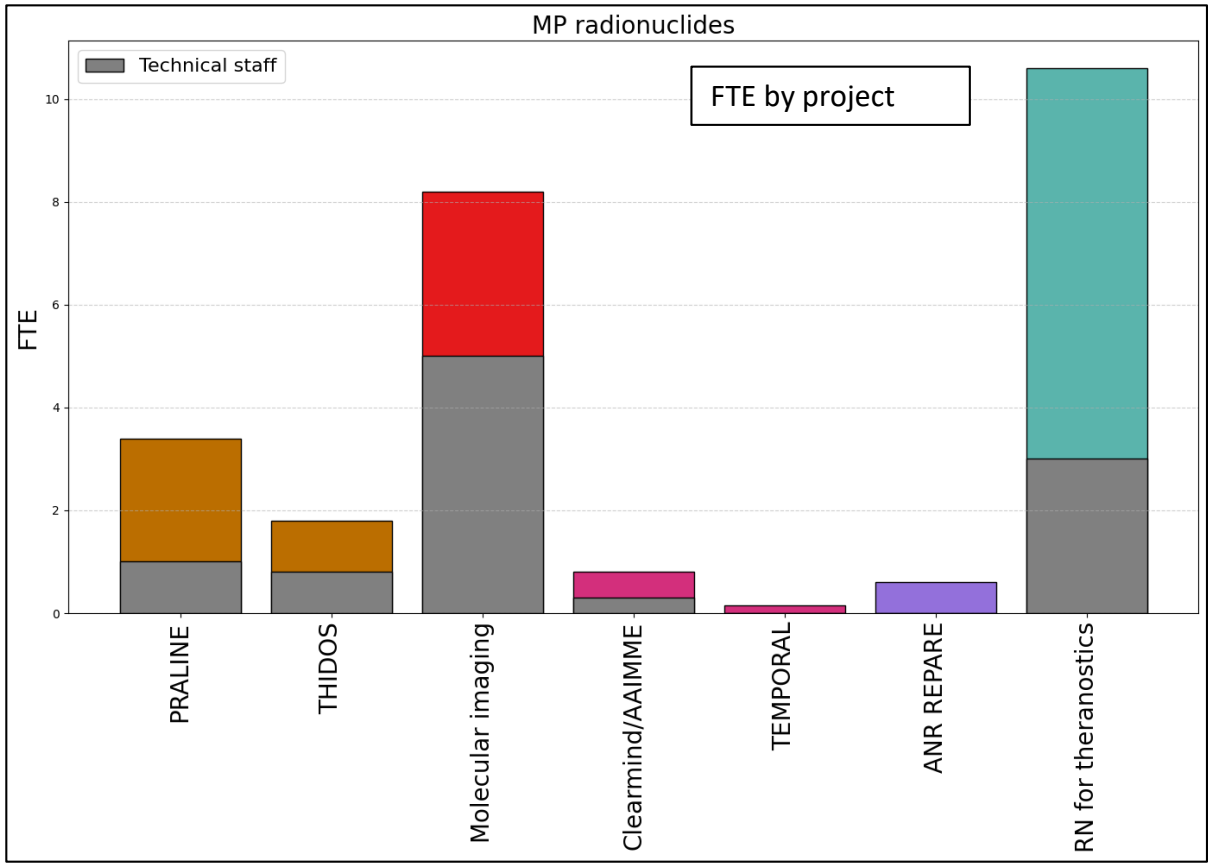


Total publications in targeted therapies MP: 34

Total fundings in targeted therapies MP: 152 kEuros in2p3, 1267 kEuros non-in2p3

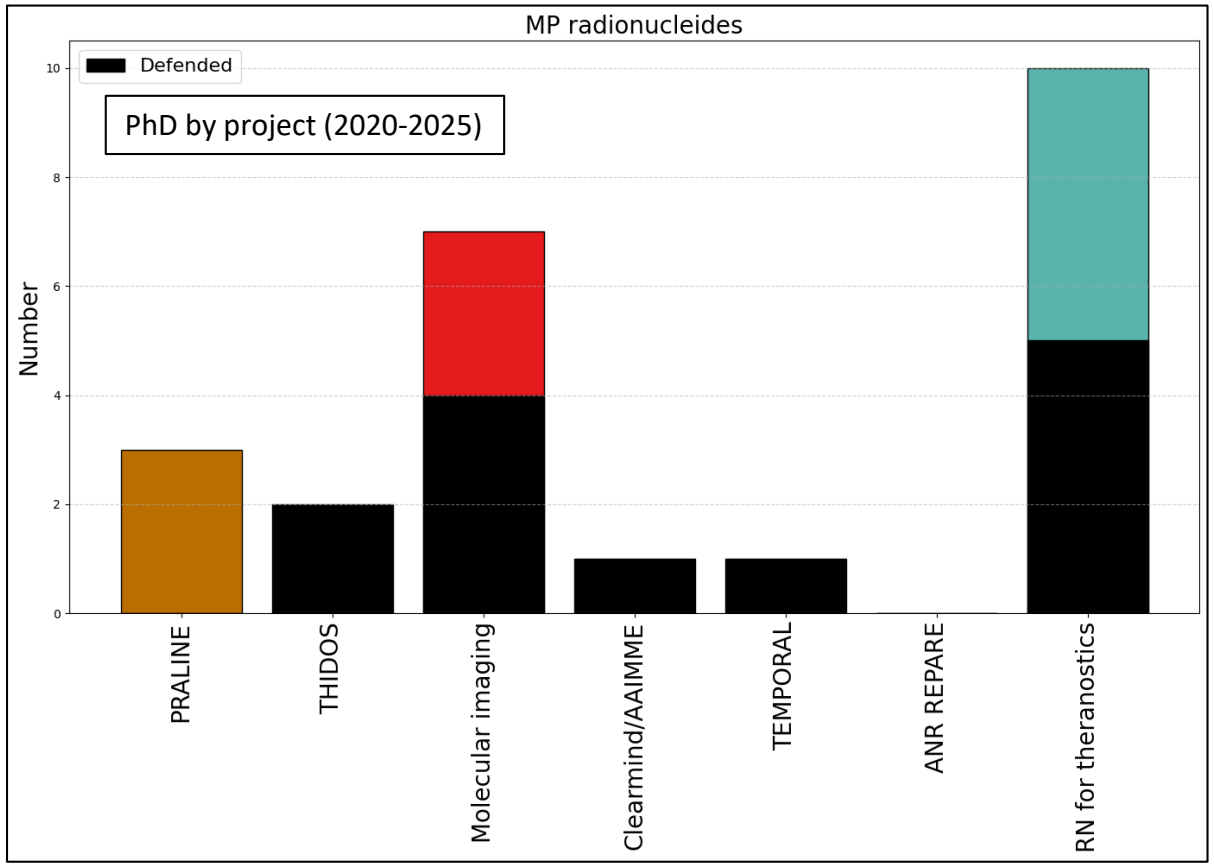
FTE in the radionucleides Master-project of **in2p3**



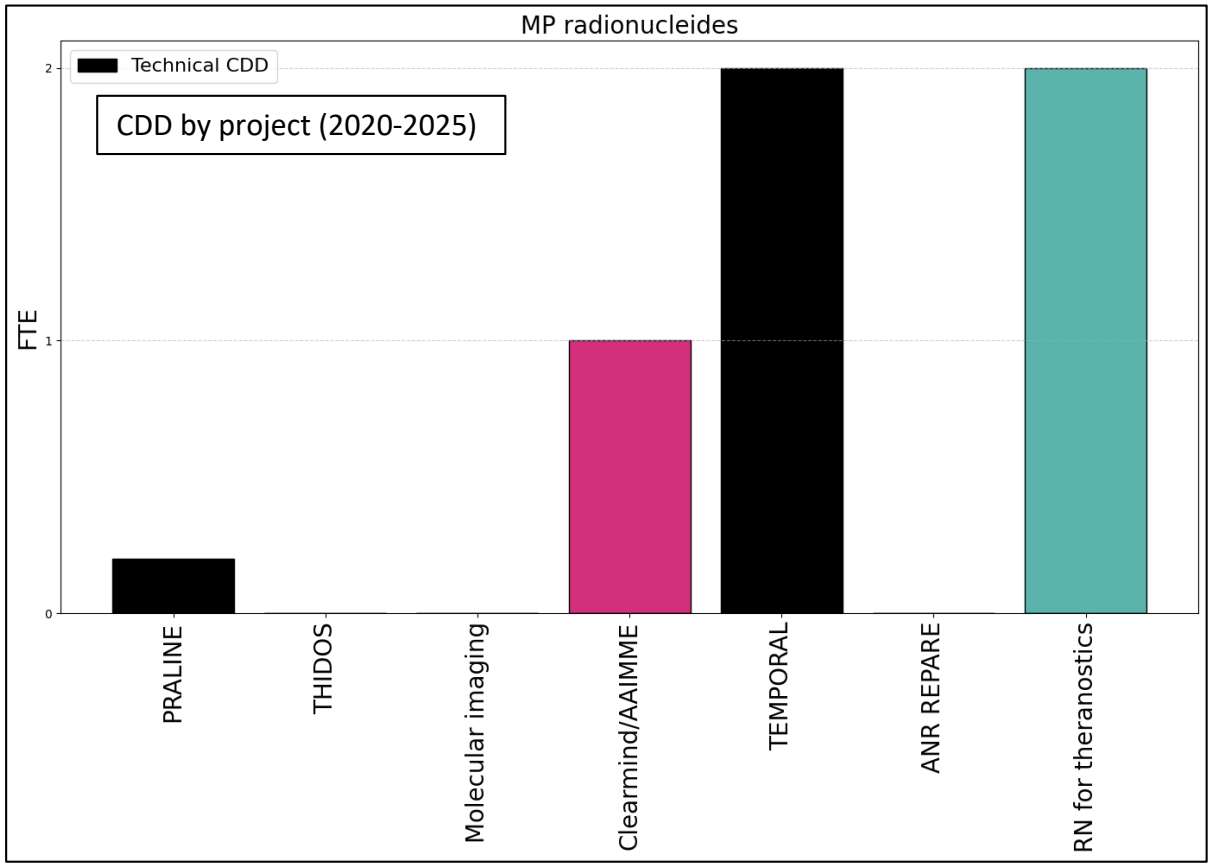


Total FTE in RN MP: 15.46 researchers, 10.10 technical staff

FTE in the radionucleides Master-project of **in2p3**

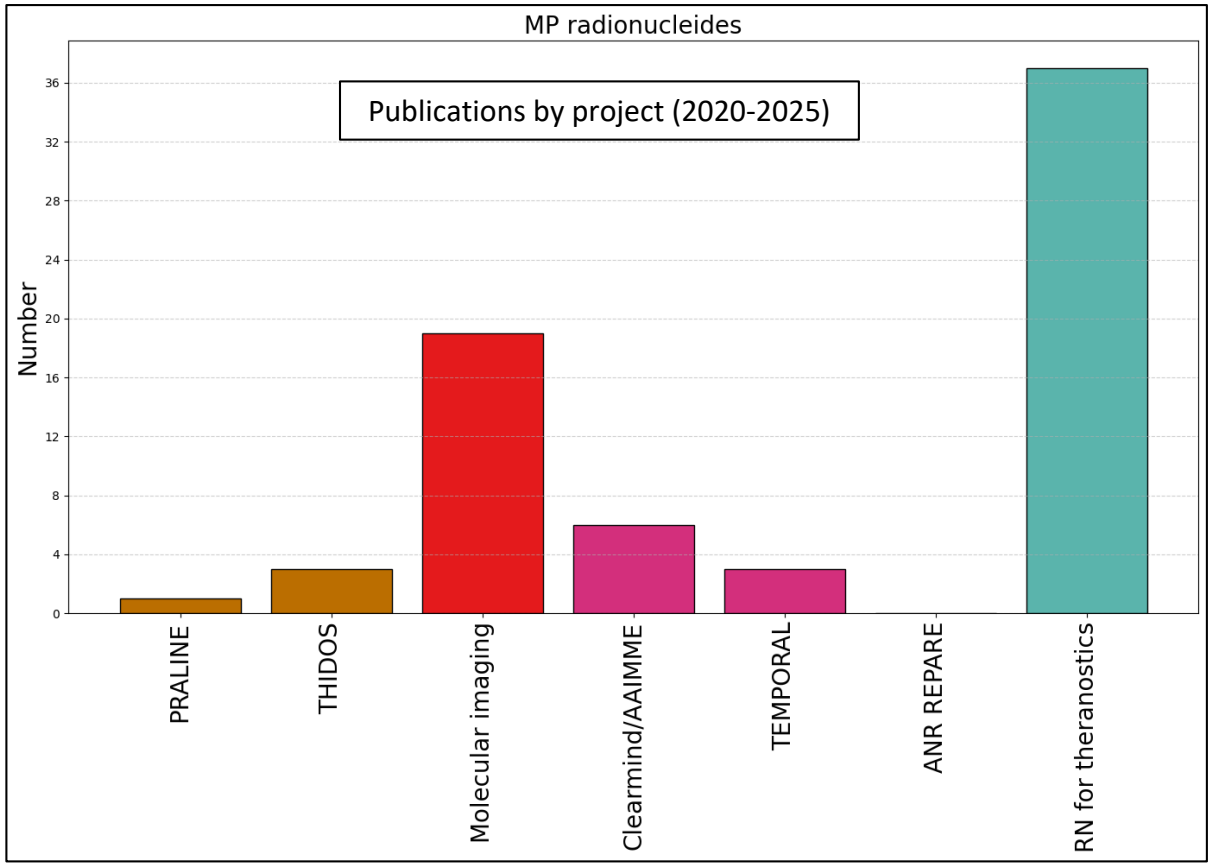


Total PhD in RN MP: 13 defended, 11 on-going

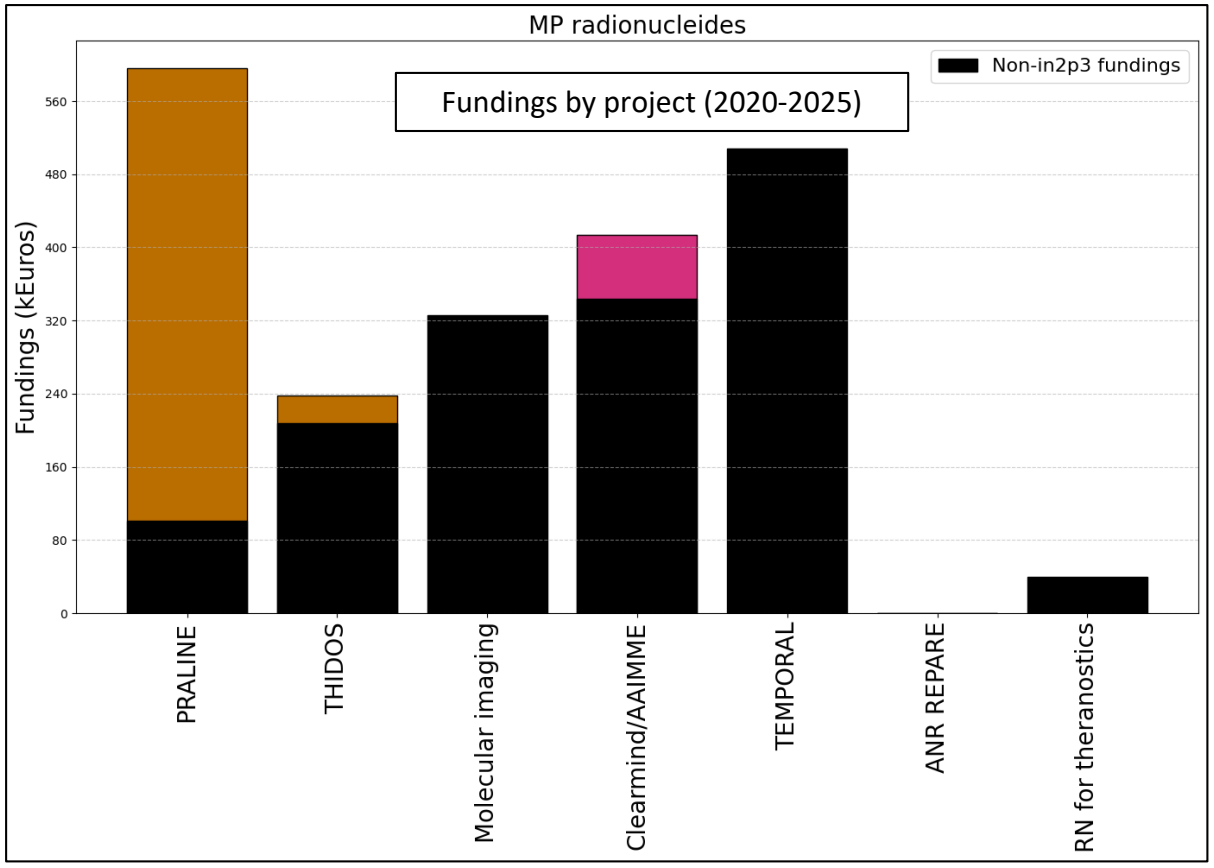


Total CDD in RN MP: 3 FTE researchers, 2.2 FTE technical staff

Publications & fundings in the radionucleides Master-project of **in2p3**



Total publications in RN MP: 69



Total fundings in RN MP: 152 kEuros in2p3, 1267 kEuros non-in2p3