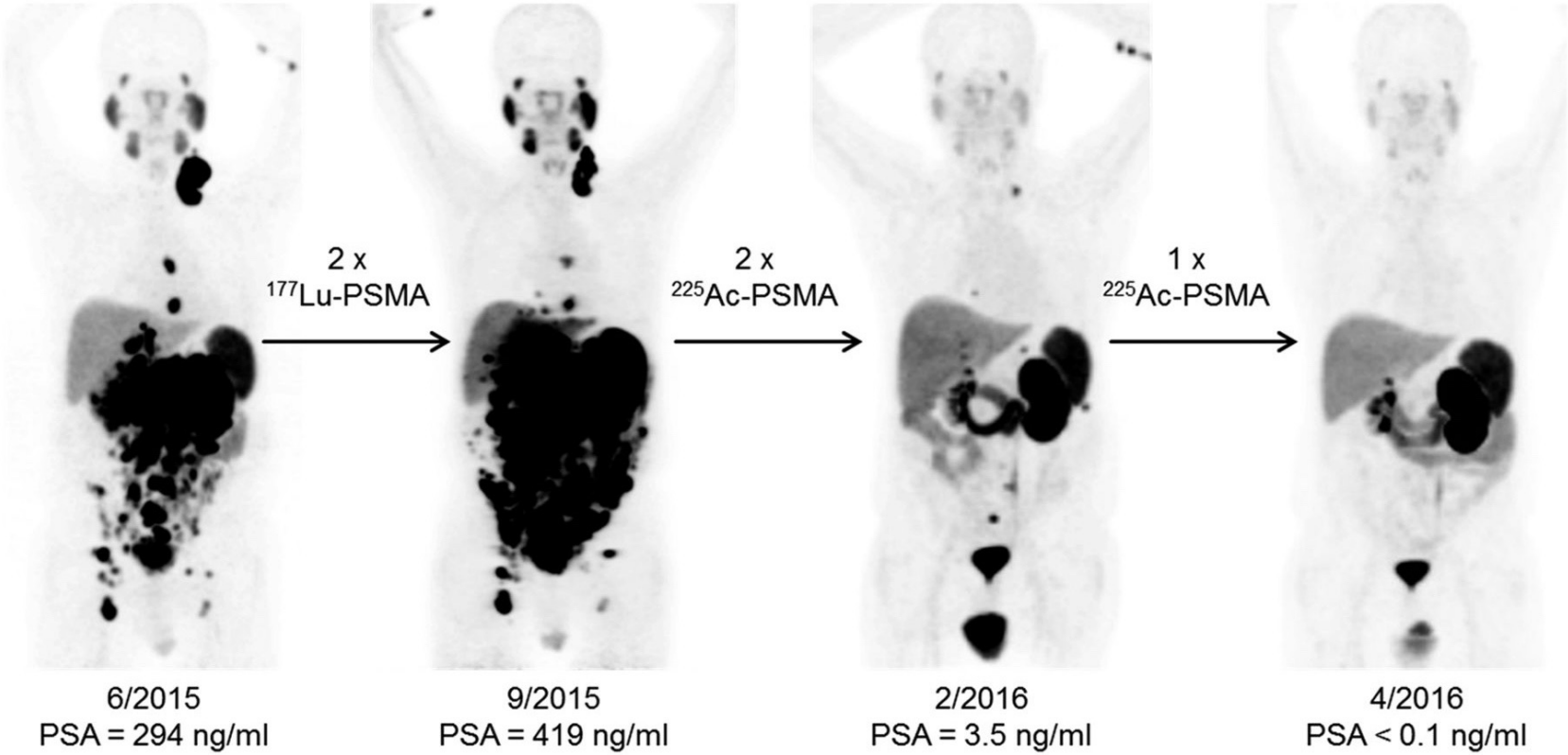
THE EUROPEAN MEDICAL RADIONUCLIDES PROGRAMME
A SHORT INTRODUCTION

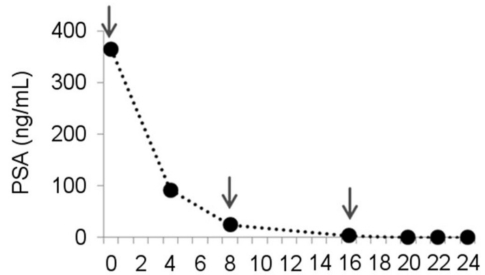
Lisbon

Thierry Stora, CERN

27 Nov 2023

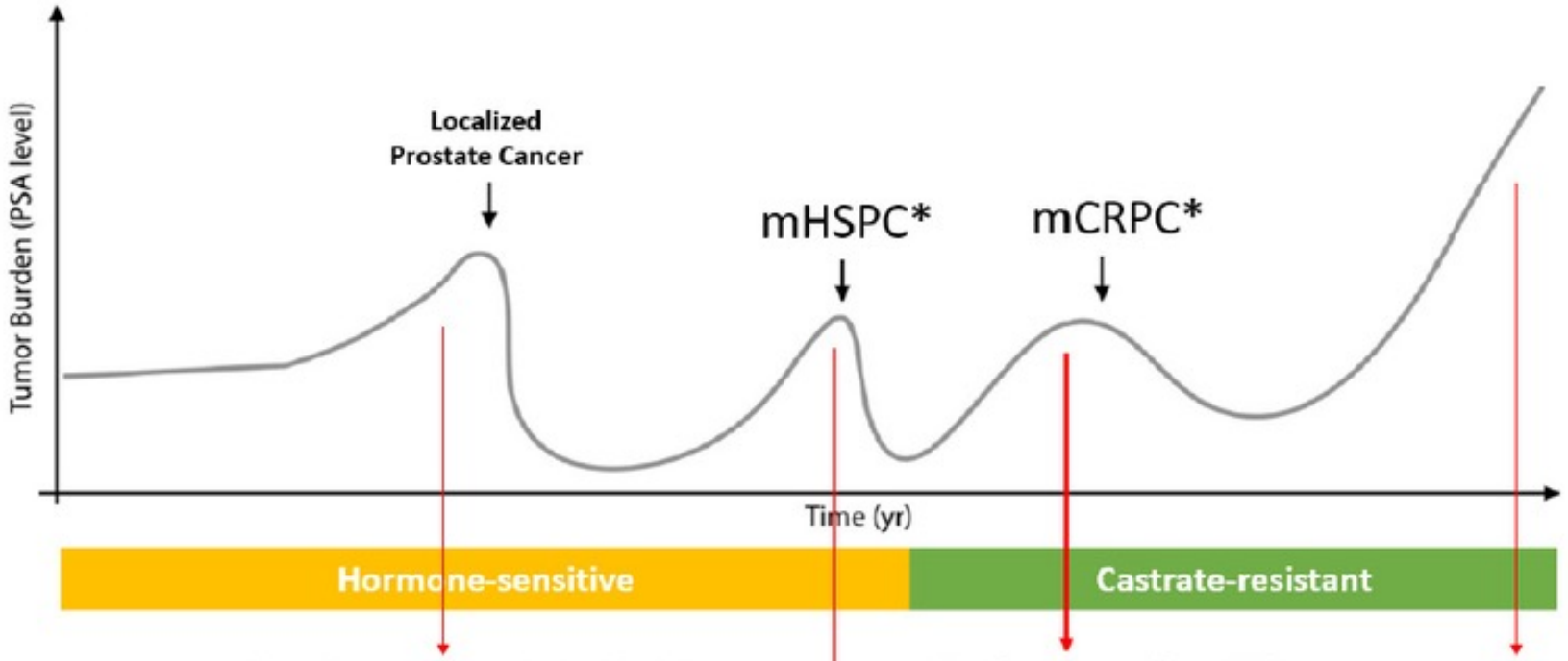
^{225}Ac-PSMA in Targeted Alpha Therapy





C. Kratochwil, *et al.* J. Nucl. Med. 57, 1941 (2016).
225Ac-PSMA-617 for PSMA-targeted α-radiation therapy of metastatic castration-resistant prostate cancer

PSMA Theranostics Clinical Trials



Neoadjuvant therapy for localized disease

1. ^{177}Lu-PSMA-617 (LuTectomy)

First-line therapy for mCRPC

1. ^{177}Lu-PSMA-I&T (Bullseye)
2. ^{177}Lu-PSMA-617 + enzalutamide (ENZA-P)
3. PSMAfore

First-line therapy for mHSPC

1. ^{177}Lu-PSMA-617 (UpFrontPSMA, PSMAddition)

Second-line or later therapy for mCRPC

1. ^{177}Lu-PSMA-617 (LuPSMA,TheraP, VISION)
2. ^{177}Lu-PSMA-617 + olaparib (LuPARP)
3. ^{177}Lu-PSMA-617 + pembrolizumab (PRINCE)
4. ^{177}Lu-PSMA-I&T (SPLASH)
5. ^{225}Ac-PSMA-617 (AcTION)
6. ^{177}Lu-J591 (NCT00538668)
7. ^{225}Ac-J591 (NCT04506567)
8. ^{227}Th-PSMA-TTC (NCT03724747)
9. ^{131}I-MIP-1095 + enzalutamide (ARROW)
10. ^{177}Lu-PSMA-R2 (NCT03490838)

*mHSPC (metastatic hormone-sensitive prostate cancer)
*mCRPC (metastatic castrate-resistant prostate cancer)
*Different colours represent various PSMA-targeted radiopharmaceuticals (^{177}Lu-PSMA-617, ^{177}Lu-PSMA-I&T, ^{177}Lu-J591, ^{225}Ac-J591, ^{227}Th-PSMA-TTC, ^{131}I-MIP-1095, ^{177}Lu-PSMA-R2)

Poor prognosis of metastatic prostate cancer

17 theranostics clinical trials (as of 2021)

Zhang,et al. Cancers 2021, 13, 4023.

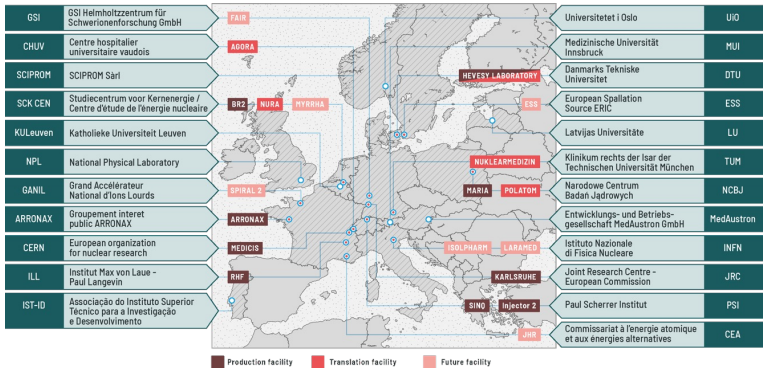
Courtesy prof MD J. Prior, CHUV

Are there other research medical radionculides ?
PRISMAP.EU - The European medical radionuclides programme in a nutshell

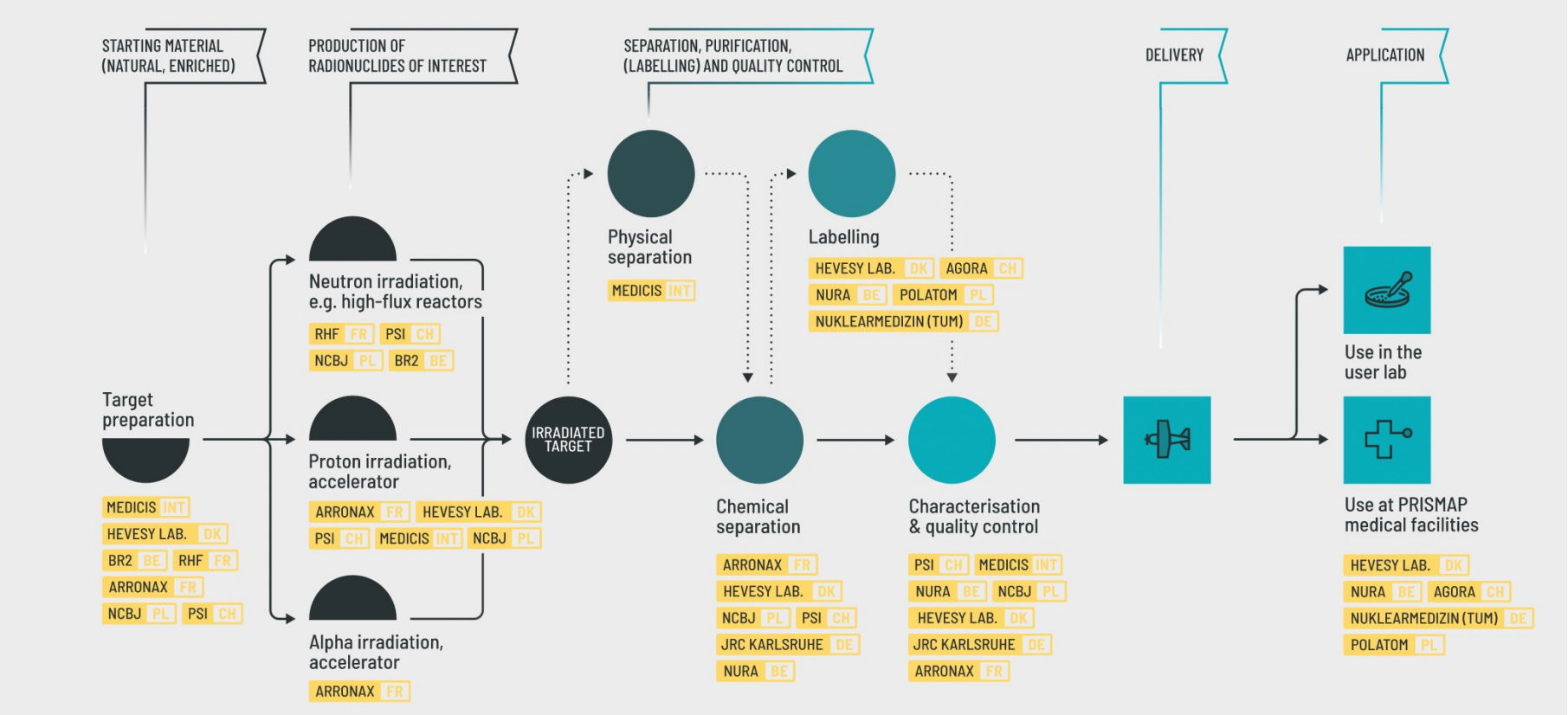
- Our web interface : https://www.prismap.eu/radionuclides/portfolio/

43 Sc Scandium	44 Sc Scandium	47 Sc Scandium	52 Mn Manganese	64 Cu Copper	67 Cu Copper	103 Pd Palladium
111 Ag Silver	128 Ba Barium	128 Cs Caesium	135 La Lanthanum	153 Sm Samarium	149 Tb Terbium	152 Tb Terbium
155 Tb Terbium	161 Tb Terbium	165 Tm Thulium	165 Er Erbium	169 Er Erbium	175 Yb Ytterbium	199 Au Gold
203 Pb Lead	211 At Astatine	213 Bi Bismuth	223 Ra Radium	224 Ra Radium	225 Ac Actinium	227 Th Thorium

Parameter	Specification
Half-life	4.04 h
Daughter	Stable Ca-44
Branching Ratio/Decay	94.3% β^+, 5.7% EC
Production	Ca-44(p,n)Sc-44 [or Ca-44(d,2n)Sc-44 at ARRONAX]
Purification	1 or 2 steps column separation
Chemical Form	In 0.05 M HCl, 0.1 M HCl, 4.85 M NaCl/0.13 M HCl or 1 M NaOAc
Specific Activity	2 GBq/mg
Radionuclidic Purity	99.8% (0.2% Sc-44m)
Radiochemical Purity	Labelling up to 25 MBq/nmol DOTANOC or DOTATATE
Identification	1157 keV gamma line present
Appearance	Clear and colourless solution
pH	Depends on chemical form
Activity available	Up to 1 GBq
Availability	On demand
Grade	Research grade or preclinical grade, n.c.a.



Supply chain in the back of PRISMAP



https://www.prismap.eu/radionuclides/portfolio/153Sm/

Chemical properties

Sm-153 is a radiolanthanide, usually in trivalent state. It can be radiolabelled with macrocyclic chelators, in particular DOTA. The ionic radius is 95.8 pm.

Nuclear properties

Sm-153 decays by β^- decay with a half-life of 1.9285(2) days to stable Eu-153. It emits a low to medium energy β^- spectrum with 225 keV average energy and 808 keV maximum energy. In addition to β^- emission it shows ample emission of low energy conversion and Auger electrons, thus emitting in total about 2.34 electrons (with energies above 4 keV) per decay.

Moreover, Sm-153 emits γ-rays at 103 keV (29.14%) suitable for SPECT imaging.

The mean electron energy emitted per decay is 265 keV, the mean photon energy per decay is 62 keV.

Production

Sm-153 is produced by thermal neutron irradiation of enriched Sm-152 oxide targets in the BR2 reactor at SCK CEN. The produced carrier-added Sm-153 is then mass separated at the MEDICIS facility at

Purity grades available

PRECLINICAL

No carrier added (n.c.a.)

Available in n.c.a. form (but n
specific activity)

Full specifications

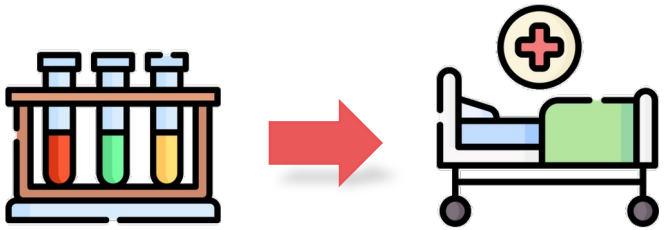
Applications

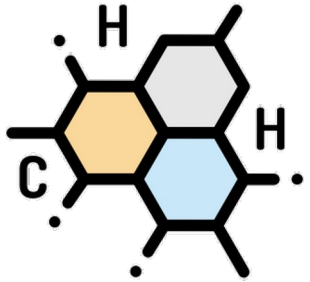
- β-therapy
- SPECT

Point of supply

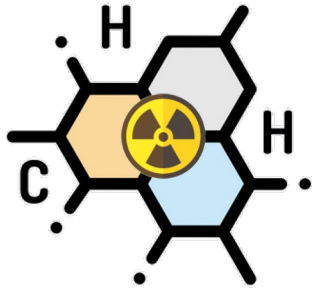
Parameter	Specifications
Production route	Sm-152(n,γ)Sm-153
Daughter	Decays to stable Eu-153: 100% β^-
Half-life	1.93 d
Processing	Off-line mass separation (CERN-MEDICIS) + 3-step column separation
Primary Container	2.5 mL borosilicate glass V-vial with silicon rubber screw cap
Product Grade	n.c.a. (but not in theoretical molar activity)
Physical Form	Liquid or solid deposit
Chemical Form	In 0.05 M HCl (evaporation to dryness is also possible)
Radioactive Concentration (gamma spectrometry)	> 50 MBq/ml
Appearance	Clear colourless solution
Radionuclide identification (gamma spectrometry)	70 keV, 97 keV and 103 keV gamma lines present
Radionuclidic Purity (gamma spectrometry)	>99.99%
Chemical purity (ICP-OES)	n.a.
Molar activity (ICP-OES)	280 GBq/μmol Sm at time of mass separation (>11% of theoretical maximum)
Apparent Molar Activity	Labelling up to 50 MBq/nmol p-SCN-Bn-DOTA and DOTATATE
Microbiological quality	n.a.

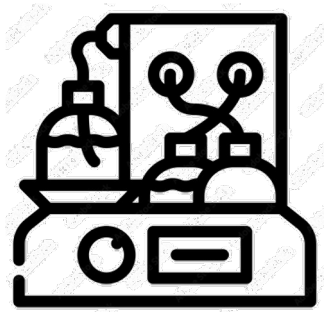
Experimental services





Vector & chelator



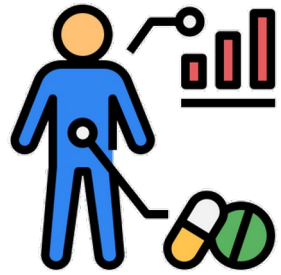


Radiolabelling & QC

Preclinical studies

Regulatory documents for clinical studies

GMP manufacturing and documentation



Clinical trial

Where are the projects coming from ?

https://www.prismap.eu/access/user-projects/

BELGIUM

In vivo cellular & molecular imaging lab (ICMI)
VU Brussels

Imaging and Pathology
KU Leuven

Molecular Imaging Center
Antwerp

CZECH Rep.

GERMANY

Pharmaceutical Radiochemistry
TU Munich

Radiopharmaceutical Cancer Research
Dresden (/CZ)

FRANCE

UGA – Inserm
La Tronche

CEMHTI Radiochemistry
Orleans

Inserm
Montpellier (/PT)

Radiopharmacy
Bordeaux

Radiochemistry
Hopital Frederic Joliot
Orsay

PORTUGAL

ITALY

Fondazione IRCCS Istituto Nazionale dei Tumori
Milano

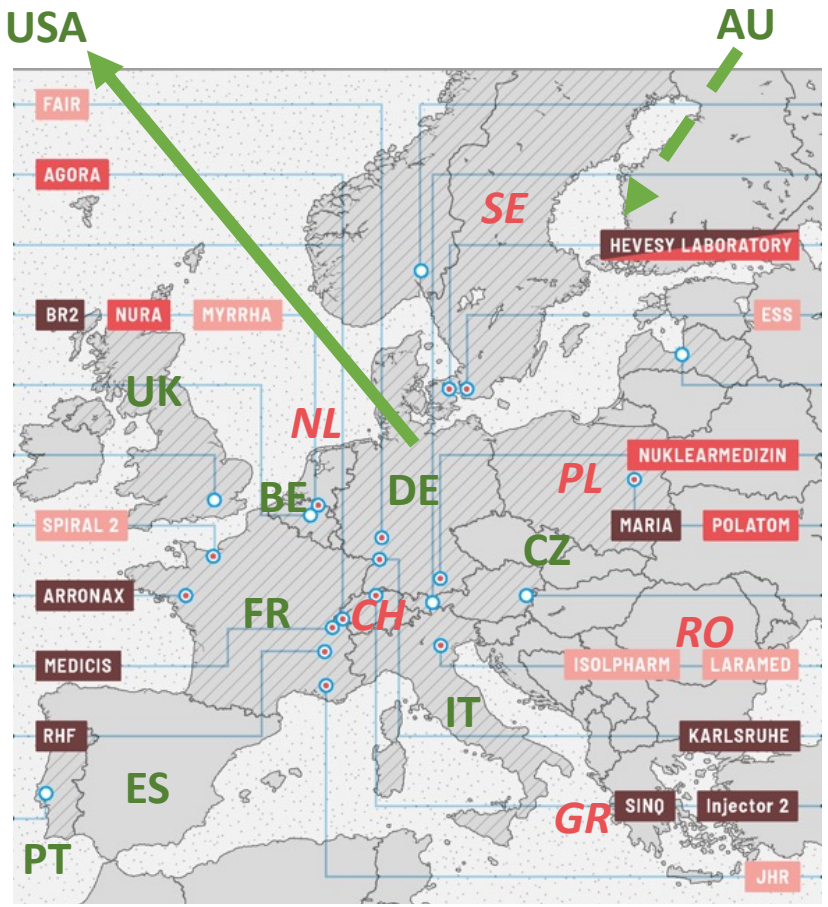
Dep Molecular Biotechnology Health Sciences,
Torino

SPAIN

Radiochemistry unit,
Hospital Gregorio Marañón
Madrid

UK

Biomedical Engineering and Imaging Science
London



https://www.prismap.eu/access/user-projects/

+17 projects selected in a single call last week !

1st publication accepted in JNM

Terbium-161 over Lutetium-177 more stable GRPR Ligand– A Preclinical Evaluation

Improved FAP-radiotheranostics for personalized cancer treatment (211At)

Phantom measurements quantitative 225Ac- (micro)SPECT imaging (213Bi)

Feasibility of increased 211At production by 210Po assessment

Imaging of 165Er

Selective oncological theragnostic based on exosomes (161Tb)

161Tb-PSMA cell targeting treatment of prostate cancer biochemical recurrence

Dual 152Tb/149Tb radiolabeling for diagnostic and theranostic applications

Zebrafish embryo as a novel model to evaluate the efficacy of short range emitters used for targeted radionuclide therapy

New chelators for complexation of medically useful lanthanide and actinide radioisotopes

Our objectives

- Provide access to new radionuclides and new purity grades for medical research
- Create a common entry port and web interface for the starting research community
- Enhance clarity and regulatory procedures to promote research with radiopharmaceuticals
- Unlock the biomedical research through better data on radionuclides
- Ensure the long-term sustainability of PRISMAP

27 EU

PRISMAP

Medical Radionuclides

WWW.PRISMAP.EU/RADIONUCLIDES/USER-FORUM/

WWW.PRISMAP.EU

@MEDRADIONUCLIDE

PRISMA

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