Theranostic radiopharmaceuticals for imaging/treatment of cancer

MEDICIS-Promed Work Package 3

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Introduction

Work package 3 (WP£) is one ofthe three work packages within MEDICIS-Promed. It consists of 5 out of a total of 15 Early stage Researchers (ESRs) and one work package leader who are all working at various places in Europe.

WP3 – Leader + ESRs positions

WP leader: Ilyes Zahi
ESR1. Annie Ringvall Moberg
ESR6. Roberto Formento Cavaier
ESR8. Alice D'Onofrio
ESRCH2. Francesco Cicone
ESRCH3. Ioanna Prionisti

Objectives of WP3

- Optimised and industrial performant production of new radioisotopes for theranostic using mass separation technology.
- Synthesis and design of bio-conjugated molecules for the specific DNA-targeting of tumor cells.
- Radioimmunotherapy and biodistribution studies on small animals as a proof of concept of the chosen radionuclides.

ESRs and their projects

ESR1. Annie Ringvall Moberg

In order to further develop ion sources and target units at ISOLDE, CERN, a non-radioactive test laboratory, Off-line 2, is currently under construction. Off-line 2 will also allow for improvements of beam manipulation techniques using a Radio-Frequency Quadrupole Cooler and Buncher (RFQCB). My primary task will be to take part in the construction and commissioning of Off-line 2 along with the RFQCB and also to further develop and improve the RFQCB.

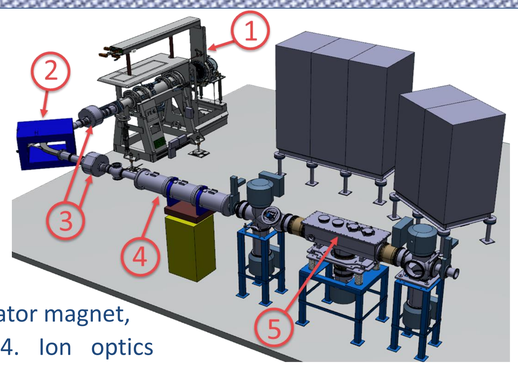


Figure of Off-line 2.
1. ISOLDE Front-end,
2. 90 degree mass separator magnet,
3. Beam diagnostics, 4. Ion optics (quadrupole triplets), 5. RFQCB.
Image: Stuart Warren

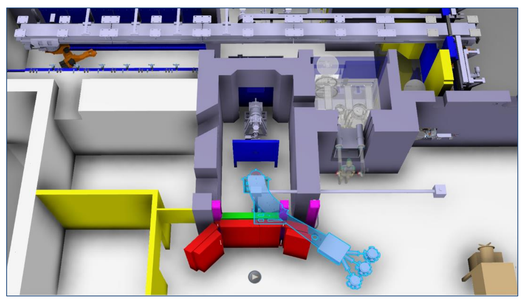
A part of the RFQCB assembly at the ISOLDE Off-line 2 facility.

ESR6. Roberto Formento Cavaier

The objective of this work is to study the production of innovative radionuclides such as Tb-149 using a commercial middle sized high-current cyclotron (GIP Arronax) while exploiting the technology of the mass separator developed within the MEDICIS-PROMED project at CERN.

Arronax IBA C70 cyclotron, Nantes

+

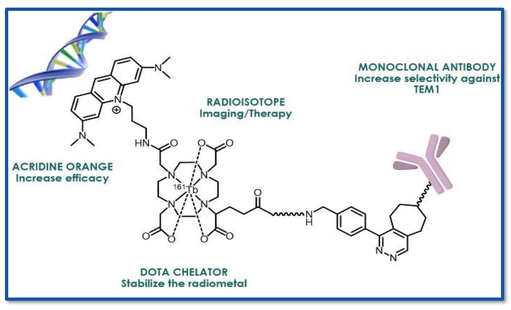


CERN-MEDICIS mass separator (light blue)

= **PRODUCTION OF** HIGH SPECIFIC ACTIVITIES **INNOVATIVES RADIONUCLIDES**

ESR8. Alice D'Onofrio

The final goal of this project is the synthesis and the biological evaluation of bifunctional compounds for theranostic applications. Those compounds, consisting of a central DOTA chelator that will stabilize the radioisotope, will be functionalized with a DNA-targeting moiety to increase the efficacy of Auger electrons and with a mAb fragment for the specific recognition of tumor cells. Furthermore, we intend to evaluate the influence of *in-vivo* click chemistry and of a bio-cleavable linker on the pharmacokinetic and biological behavior of such complexes.



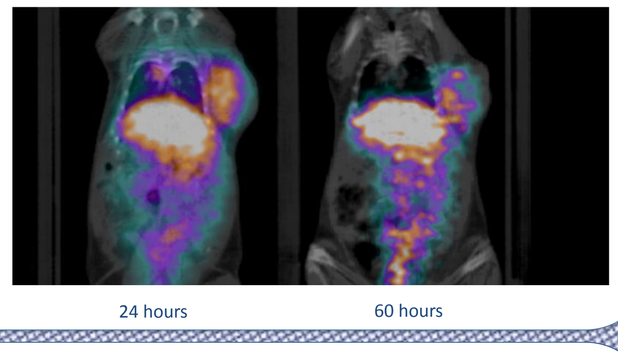
Desired bi-functional Radio-immuno conjugates

ESRCH2. Francesco Cicone

As a Nuclear Medicine physician, I am the end-user of the novel radio-immunoconjugates synthesized within the frame of the MEDICIS-PROMED with the aim of imaging and treating cancer. In particular, I will perform preliminary in vitro and in vivo tests on mouse models of human sarcoma and neuroblastoma, hopefully driving a successful translation into patient clinic.

Micro PET/SPECT/CT

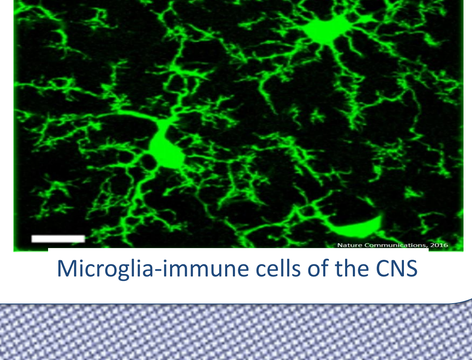
^{152}Tb-CHX-A''-DTPA-ScFv78Fc anti TEM1



24 hours 60 hours

ESRCH3. Ioanna Prionisti

The radioisotopes produced at the CERN-MEDICIS facility will be implanted in rodents to assess their efficacy for the treatment of glioblastoma. The project focuses on developing new instruments and delivery methods for brachytherapy and investigates the impact and efficiency of these methods at the cellular and organ levels. In particular, the project investigates how brachytherapy affects the brain's microvasculature and immune system.



Microglia-immune cells of the CNS

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