MEDICIS-PROMED : MEDICIS-produced radioisotope beam for medicine

Marie Curie ITN proposal – Horizon 2020

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Figure 1: Overview of the present chain of production and distribution of radioisotopes for radiopharmaceuticals (top) and activities covered in the MEDICIS-PROMED Marie-Curie ITN with possible innovations for hospitals and private companies.

Executive Summary

Pure accelerated radioisotope beams have been used for 50 years for fundamental physics such as neutrino mass determination or for nuclear structure (Nature 2013, discovery of pear shape in exotic nuclei); CERN-ISOLDE plays a central role in developing accelerator technologies and fostering collaborative approaches to advance this field of isotope mass separation online. Our recent contribution was the use of nanomaterials for more intense beam production and laser ion sources for purification that for instance lead to the discovery of the yet unknown ^{233}Francium isotope (publication ready to be submitted).

Radioactivity and radioisotopes are widely used for functional imaging in medicine using mostly ^{99m}Tc and is expected to play a major role in cancer treatment with new isotopes emitting alpha particles, as shown with the recently introduced ^{223}Radium chloride (Xofigo®) radiopharmaceutical used as treatment and pain relief drug in advanced bone cancers resistant to hormones. However, either shortage in the supply of the commonly used ^{99m}Tc or lack of access to new chemical elements with adequate radioactive emission properties is a severe treat to supply these drugs or develop personalized treatment that combining functional imaging and therapy.

Ovarian cancers have poor prognosis, are the second most frequent cancer for women and one of the deadliest. The 5-year survival rates of the advanced type III/IV, more than 60% of the diagnostics, is between 25 and 40%, significantly below the 68%, average of the 5-year survival for all types of cancers This type of cancer is difficult to treat with external radiotherapy, because of possible presence of metastasis when the cancer is diagnosed at a late stage, and because this region is difficult to irradiate without collateral damages to the neighbouring tissues. The most current cure combines chemotherapy and surgery for resection of the tumour. This type of cancer is therefore very well suited to investigate new forms of treatments, either using theranostic pairs of isotope to detect metastasis, have selective systemic radiotherapy, and possibly following the evolution of the cancer along personalized treatments. A new possible target, the tumor endothelial marker 1 (TEM1/endosialin), has been shown to be strongly expressed and is a marker of tumour vasculature for this type of cancers and others; recently, a humanized monoclonal igG antibody was shown to specifically target this marker in small animal models in preclinical imaging studies with ^{124}Iodine, and opens the route for investigations of personalized treatments combining functional imaging by PET/CT or SPECT/CT, and either alpha-emitting or beta-emitting isotopes.

MEDICIS-PROMED will train a new generation of entrepreneurial scientists, which will be able to bridge the different disciplines across fundamental research institutions, private companies and hospitals, which is required for the rapid marketing of new types of equipments and drugs used for radiopharmaceuticals in cancer treatments in hospitals, as displayed in **Fig. 1**. This will be done using radioactive ion beams that had up to now never been used to produce dedicated medical batches. This will become now possible for the first time with the construction of CERN-MEDICIS facility to extend the capabilities of the ISOLDE facility.

The training will be done in a distributed interdisciplinary network that comprises universities, international organization, national research centres, SMEs and public/private mixed entities, as shown on **Fig.2**.

The **MEDICIS-PROMED** network will train scientists in cutting edge scientific projects and apply the discoveries in companies and or directly at hospitals when appropriate. The scope of complementary projects covers the different elements required in the isotope production, acceleration, purification, delivery, radiopharmaceutical synthesis, safety, industrialisation and preclinical tests

List of partners and projects:

University of Manchester – Kostya Novoselov – growing of graphene layers on uranium/tantalum target foils for the production of new isotopes – 1 fellow

C2TN Lisbon – Prof. Goncalves - Electrospinned nanofibers to increase intensity of critical isotopes such as 211Astatine - 1 fellow

C2TN Lisbon – Prof. Dos Santos – synthesis of new radiopharmaceuticals for DNA targetting to exploit radioactivity from Auger electron emission with short range of new radiolanthanides – 1 fellow

JGU Mainz – Prof. K. Wendt – development of remotely operated solid stated laser systems for isotope purification with high efficiency; foreseen industrialization to equip medical cyclotrons – 1 fellow

KUL – Prof. P. Van Duppen – laser, mass separation – 1 fellow

CERN – MEDICIS – T. Stora, T. Giles, R. Catherall, A. P. Bernardes: isotope production, beam generation and purification, operational safety – 3 fellows

AAA Stefano Buono – GMP manufacturing, distribution – 1 fellow

CNAO, Prof. R. Orecchia : hadron therapy with PET isotopes – 1 fellow

EPFL-ISREC – Prof. Dubikovskaya, Doug Hanahan – New bioconjugates, combined fluorescence/PET imaging, animal models – 1 fellow

CHUV – Prof. Prior, Prof. Coukos: translational imaging and therapy in animals/patients – 2 fellows

HUG – Prof Buehler – Prof Ratib: robotic surgery, nuclear medicine, functional imaging – 2 fellows

Lemer-Pax : development of a type B container for transport of alpha emitters – 1 fellow

Total: 16 fellows

Hospital sofia (associated) – Prof Piperkova

NIRS / Chiba (associated), Haga-san: *PET aided hadron therapy with 11C*

Medaustron , L. Penescu (associated) : hadron therapy

ILL – U.Koester - isotope prod a reactor – radiochemistry – mass separation of isotopes produced at reactors

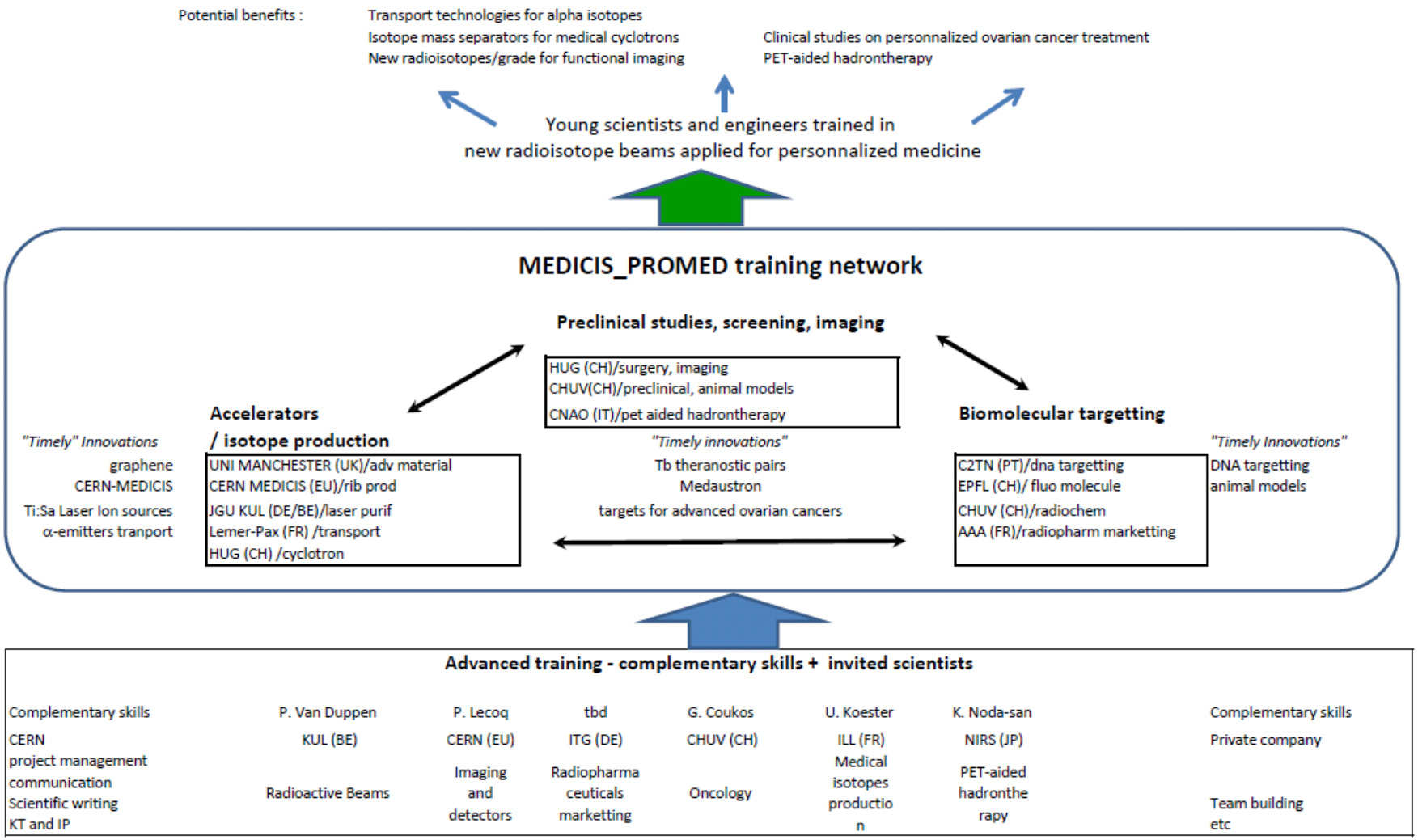

Figure 2 : Overview of the Network training activities