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| Spoke 4 – ***Preclinical and clinical breakthrough theranostic and treatments for cance***r | | | |
| Innovative therapeutic solution, with the potential to be a response for those tumours that cannot be treated with  conventional approaches. Innovation in methods of preclinical and clinical research. In particular, the pilots  dedicated to these innovations (4.4 and 4.9) will take advantage of new developments in the drug delivery  methodologies pursued by other pilots. | | | |
| **Leader** | **UNICT** | Affiliates | POLIMI, HUNIMED, UNICAL, UNIME, UNISALENTO, UNICAMP,  INFN, CANNIZZARO, BIOGEM, IOM |
| **Pilot 4.0: Leveraging biology, multi-omics and imaging data for innovative disease theranostic and**  **treatments for cancer** (UNICT, POLIMI, HUNIMED, UNICAL, UNIME, UNISALENTO, UNICAMP, INFN).  Design and development of Artificial Intelligence (AI), machine learning (ML) and deep learning (DL) models for  innovative disease theranostic and treatments for cancer (Pathology) | | | |
| **Pilot 4.1 Multifunctional materials for advanced theranostics** (POLIMI, HUNIMED, UNISALENTO).  Development of multifunctional nanocarriers for theranostic applications and for personalised medicine, to improve  targeting ability and to increase drug efficacy. Development of nanoparticles loaded with radionuclides to  implement theranostics approaches based on radio compounds (**Pathology**). | | | |
| **Pilot 4.2 Optical microsensors** (POLIMI, HUNIMED, UNISALENTO).Development of Optical microsensors for  sensing cell metabolism and cell-cell interactions in tumour models (**Pathology**). | | | |
| **Pilot 4.3 Multi-modal correlative microscopy platform**(POLIMI, HUNIMED, UNISALENTO). Development  of a multi-modal correlative microscopy platform for *in vitro*, *in vivo* and *ex vivo* biological imaging. The imaging  workflow will enable an extremely wide resolution range, spanning from the single molecule scale to clinical  imaging in the small animal model (**Pathology**). | | | |
| **Pilot 4.4: FLASH therapy effect on glioblastoma (GBM)** (UNICT, INFN, CANNIZZARO, IOM, BIOGEM).  Achievement of a biological response to FLASH and ULTRA-FLASH therapies of tumour and healthy tissues by:  1) 2D and 3D *in vitro* tumour and healthy cells response to therapy; 2) *in vivo* tumour and healthy tissues response  to therapy, in a murine and zebrafish GBM model; 3) development of complementary therapies to improve the  efficacy of treatment and quality of patient’s life (**Pathology**). | | | |
| **Pilot 4.5 Sonoporation and drug delivery for GBM and melanoma treatment** (UNICT, UNIME, INFN, IOM,  CANNIZZARO, BIOGEM). Development of a sonoporation-based systems to improve drug delivery through: 1)  synthesis of sonoporation-inducible liposomes; 2) *in vitro* tests on healthy, GBM and melanoma cell lines of  ultrasound-inducible liposomes and combination with radiotherapy; 3) evaluation of sonoporation-inducible  liposomes and radiotherapy combination in murine and zebrafish model of GBM and melanoma; 4) *ex vivo* samples analysis for conventional pathological, metabolomic, transcriptomic analyses and gene expression profile  (**Pathology**). | | | |
| **Pilot 4.6 Innovative nanoparticles for drug delivery** (UNICAL, BIOGEM). Implementation of an innovative  multiple solution developed for the treatment of cancer characterised from high expectations in terms of increase  of therapeutic efficacy and reduction of toxicity if compared to the traditional treatments (**Pathology**). | | | |
| **Pilot 4.7 Development of a perfusion-based bioreactor platform** (UNICAL, IOM). Development of a perfusion-  based bioreactor platform to successfully maintain 3D and freshly excised tissues obtained from Triple Negative  Breast Cancer patients.This platform will allow the study of the response of cancer cells in close contact with  tumour microenvironment in different controlled conditions by using an integrated approach of data from genomics, proteomics and metabolomics (**Pathology**). | | | |
| **Pilot 4.8. AI Based Systems Biology Approaches in Cancer Multi-Omics Data Analysis** (UNICAL). Design of  a platform for precision medicine able to suggest personalised treatments through the following steps: 1) database  design and multi-omics data acquisition; 2) design and development of AI models for the prediction of the multi-  omics risk score; 3) explainable AI (XAI) analysis to evaluate the predictive power of the omics parameters on the  prognosis of the patients; 4) design of a risk score based on the XAI analysis (**Pathology**). | | | |
| **Pilot 4.9 Realisation of a boron neutron capture therapy (BNCT) facility in Caserta** (UNICAMP, INFN).  Realisation of a BNCT facility in Caserta, using technology, informatics and nuclear physics methods already  available at INFN completed by the biological and clinical expertise of UNICAMP. UNICAMP will be responsible  for constructing the bunker and its services while INFN will realise the high-technology part. Installation and  commissioning will be a common activity. Research teams will address the necessary steps to integrate the  technology and the preclinical studies to enlarge the knowledge on the interaction of a mixed radiation field with  biological tissue. To this end, a set of preclinical radiobiological evaluations will be carried out by UNICAMP using existing neutron facilities while INFN will complete and install the necessary technology to produce the neutron beam. Targets will be GBM, but also head&neck, gastrointestinal, genito-urinary and gynaecological tumours based on the natural sensitivity to the radiotherapy (**Pathology**). | | | |