ERA PerMed

NEWSLETTER 3

January 2020

Austria, Belgium, Canada, Croatia, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Latvia, Luxembourg, Norway, Poland, Romania, Slovenia, Spain, Sweden, The Netherlands, Turkey

ANNOUNCEMENTS

ERA PerMed Joint Transnational Call 2020!

"Multidisciplinary Research Projects on Personalised Medicine – Pre-/Clinical Research, Big Data and ICT, Implementation and User's Perspective"

Submission deadline for preproposals: March 5th, 2020

For more details *press here*

ICPerMed-ERA PerMed Joint Internal Sustainability Workshop

May 6th, 2020
Stockholm, Sweden

Save the Date! ICPerMed Conference 2020

15-16 October, 2020
Paris, France

ERA PerMed Results of the Joint Transnational Call 2019

Personalised Medicine: Multidisciplinary Research Towards Implementation

22 successful consortia are funded with a total investment of more than 24.5 million Euros for three years

www.erapermed.eu is funded under the ERA-NET Cofund scheme of the Horizon 2020 Research and Innovation Framework Programme of the European Commission Research Directorate-General, Grant Agreement No. 779282.

According to the new EU General Data Protection Regulation (GDPR) the ERAPerMed webpage informs on respective policies.

Joint Transnational Call for Proposals 2019:

"PERSONALISED MEDICINE: MULTIDISCIPLINARY RESEARCH TOWARDS IMPLEMENTATION"

To align national research strategies, promote excellence, reinforce the competitiveness of European players in Personalised Medicine (PM), and enhance the European collaboration with non-EU countries, 31 funding organisations from 22 countries agreed to launch the second ERA PerMed Joint Transnational Call (JTC) for collaborative innovative research projects in PM. With the Joint Transnational Call for Proposals 2019 on "PERSONALISED MEDICINE: MULTIDISCIPLINARY RESEARCH TOWARDS IMPLEMENTATION", ERA PerMed fosters research and innovation activities that build close linkages between basic biomedical research, clinical research, physical sciences and bioengineering, bioinformatics and biostatistics, epidemiology, socio-economic research, as well as research on the integration of PM into clinical practice and on ethical, legal and social implications across the participating countries and beyond. Compared to the JTC2018, an additional Research Area 3 "Research towards Responsible Implementation in Health Care" was added.

Four additional funding organisations, which are not part of the ERA PerMed Consortia, joined the JTC2019: The Academy of Scientific Research and Technology (ASRT) from Egypt; the General Secretariat for Research and Technology (GSRT) from Greece; the Tuscany Region, (TuscReg) from Tuscany (Italy) and The Scientific Foundation of the Spanish Association Against Cancer (FCAECC), Spain.

189 eligible pre-proposals were submitted, 56 consortia were invited to submit a full-proposal and **22 proposals with a total funding amount of 24,634,851 € will be funded!**


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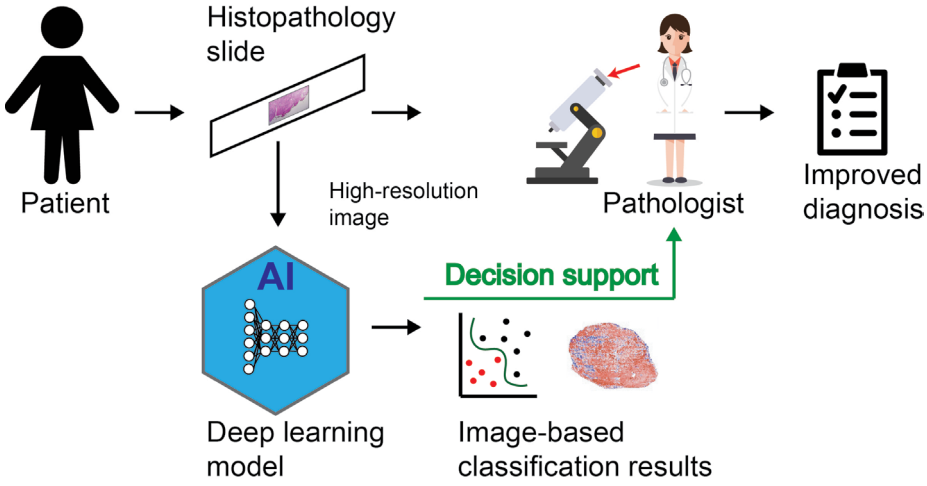
ABCAP

Advancing Breast Cancer histopathology towards AI-based Personalised medicine

Manual histopathological assessment of biopsies or resected tumours is the main mode to detect breast cancer and to establish diagnosis. However, there is a shortage of pathology expertise and a high inter-assessor variability between pathologists. This leads to prolonged response times and unequal access to top-quality assessments. Misclassifications cause both over- and under-treatment, and can have severe consequences for individual patients.

In the ABCAP programme we will develop and validate novel state-of-the-art deep learning-based computer models for improved routine histopathology classification and for refined patient stratification. ABCAP is based on large population samples to ensure representative models. Through comprehensive validation of the developed models, evidence for clinical translation will be established. Improved quality of breast cancer histopathology assessments will contribute towards reducing both over- and under-treatment of breast cancer patients.



The ABCAP consortium is developing novel deep learning-based computer models to improve breast cancer diagnosis based on histopathology image data.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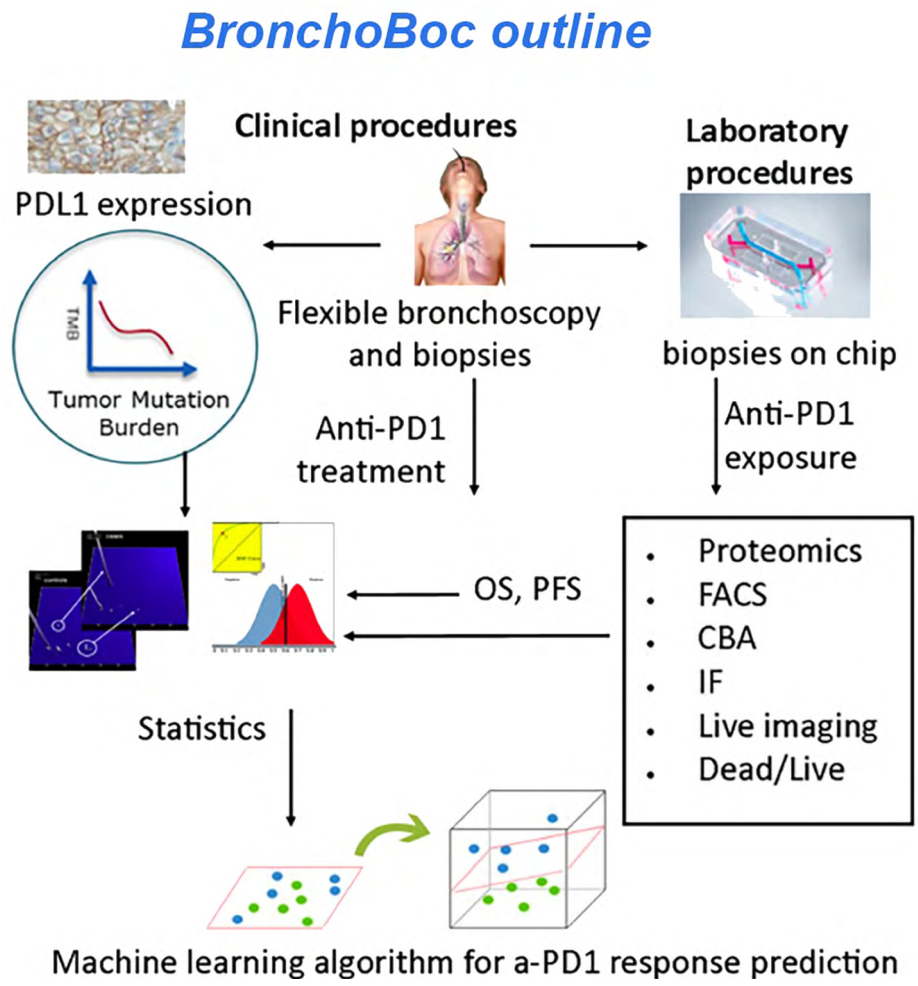
BronchoBOC

Proteomic screening of bronchoscopic Biopsies-On-Chip for improved prediction of anti-PD-1 responses in real-time

Anti-PD-1 first-line monotherapy is indicated for patients with advanced non-small-cell lung cancer (NSCLC), non-targetable driver mutations and >50% PDL1 expression. Still, the majority of patients do not respond or become resistant after initial response. Identifying patients who will benefit from anti-PD-1 monotherapy or need more aggressive combinatorial treatment is an unmet need. Our aim is to develop the first three-dimensional bronchoschopic biopsies-on-chip (BronchoBOCs) to predict real-time responses to PD1-blockade in NSCLC patients. We will conduct a prospective multicentric exploratory clinical trial by studying in parallel clinical benefits of NSCLC patients to a-PD1 monotherapy matched to responses of their BronchoBOCs. We will acquire profiles, by using mass spectrometry proteomics (LC-MS/MS), FACS, cytometric bead arrays and imaging. Machine learning approaches will be allied to BronchoBOC profiles and clinical data to identify the best predictive biomarker patterns.



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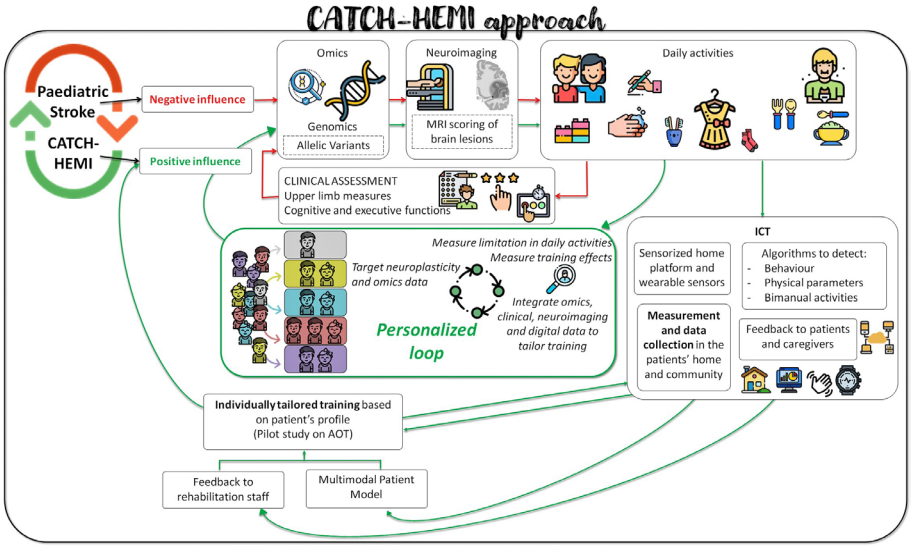
CATCH-HEMI

Combining biomArkers and Tele-health solutions for delivering at home and in the Community precision medicine and intervention for the upper limb in cHildren with HEMIplegia due to stroke

Hemiplegia due to stroke is a common condition in childhood, affecting up to 1 child in 1,000 life birth with a severe impact on children's quality of life. CATCH-HEMI aims to change the current management of these children by identifying relevant biomarkers of four different areas (omics, clinical, neuroimaging, digital data) to create a novel transdisciplinary patient-centred model to optimize and tailor their rehabilitation treatment. The feasibility of CATCH-HEMI approach will be applied for deeply analysing big data and understanding results of previous researches and in new pilot studies on already available rehabilitative treatments. The results will provide an example of how different kinds of biomarkers can contribute to create a plan for the management of children with hemiplegia, thus leading to a better understanding of the correlation between genetic and phenotypic data. The Health Technology Assessment will provide estimates of its national and regional cost effectiveness.

The following patient associations are supporting the CATCH-HEMI project:
- FightTheStroke, Italy
https://en.fightthestroke.org
- Fondation Paralysie Cerebrale, France
https://www.fondationparalysiecerebrale.org/en
- New Vision Organization, Egypt



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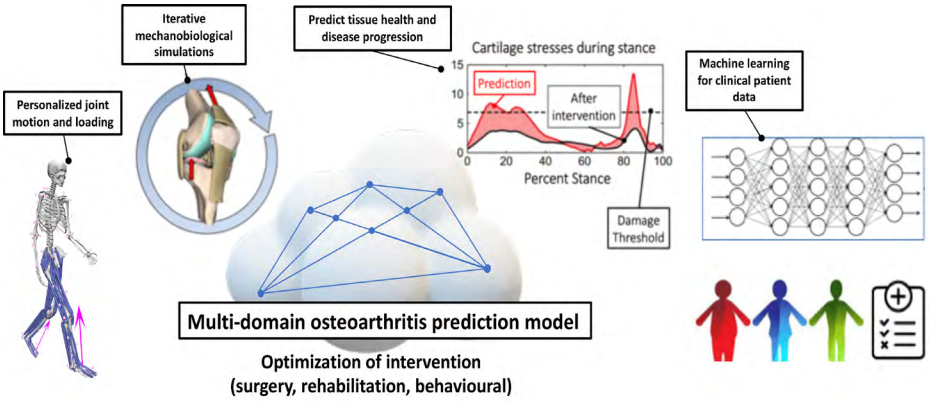
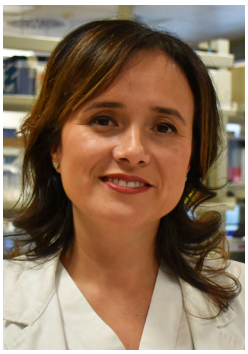
DEEPMECHANOKNEE

A novel tool for personalised and socio-economically optimal treatment planning for patients with osteoarthritis

Osteoarthritis is the most common joint disease affecting over 40 million Europeans. There is no cure for the disease. Thus, the most effective treatment for the disease would simply be prevention. That is currently problematic and proper preventive actions should be guided by personalised prediction of the disease progression.
The aim of the DEEPMECHANOKNEE project is to develop an accurate and fast method to predict the progression of knee osteoarthritis over time.
In the novel method, a multi-scale biomechanics and computational modelling, imaging, and clinical data are combined with a deep learning algorithm. Through simulations, the method can indicate (optimize) the best possible personalised treatment for a patient that could ultimately prevent or delay the progression of knee osteoarthritis. The treatment could be a changed lifestyle, tailored rehabilitation, or a specific surgical intervention. The socio-economic impact of this approach is expected to be significant.

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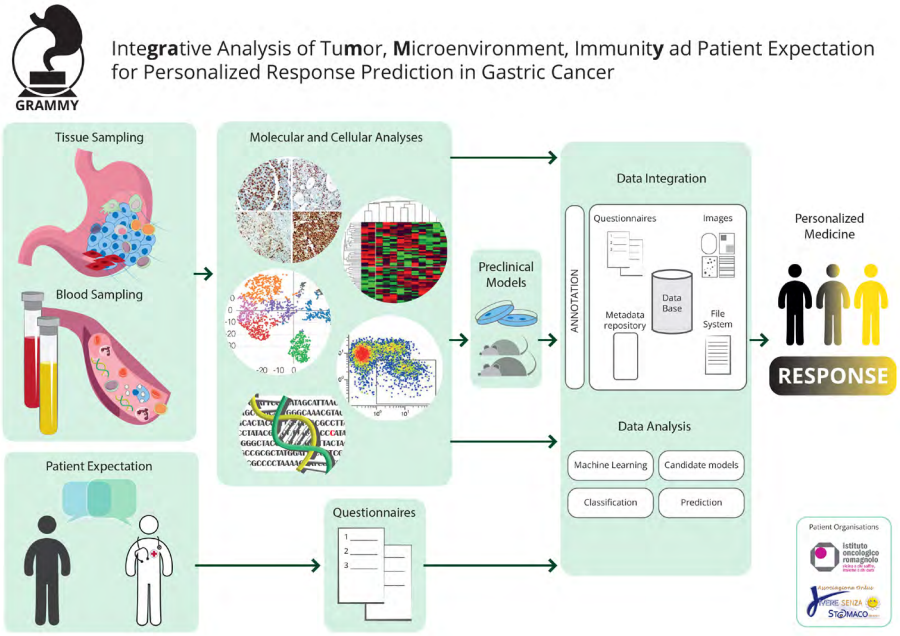
GRAMMY

InteGRAtive analysis of tuMor, Microenvironment, immunitY and patient expectation for personalised response prediction in gastric cancer

Gastric cancer (GC) is a complex and heterogeneous disease that represents the third leading cause of cancer death in both sexes worldwide. GC management is hindered by the limited efficacy of current therapies and it is thus mandatory to develop novel strategies and identify predictive markers for the stratification of patients expected to benefit from targeted therapies.
GRAMMY proposes a novel multilevel approach integrating high impact basic, translational and psychological/social research towards developing an optimized patient stratification tool for the early prediction of therapy-resistant GC patient groups. Targeted actions aim to: determine comprehensive profiles of cellular, molecular and immune phenotypes of GC tumours; validate non-invasive tools for treatment monitoring; develop patient-specific drug-response pre-clinical models; determine each patient's psycho/sociological and physician-patient interaction profiles and develop a personalised prediction tool by integrating each patient's biological and psycho/sociological traits. Integration of such multi-nodal data represents a challenge towards identifying the putative links between disease-specific cellular and molecular characteristics, patient perception and therapy response.

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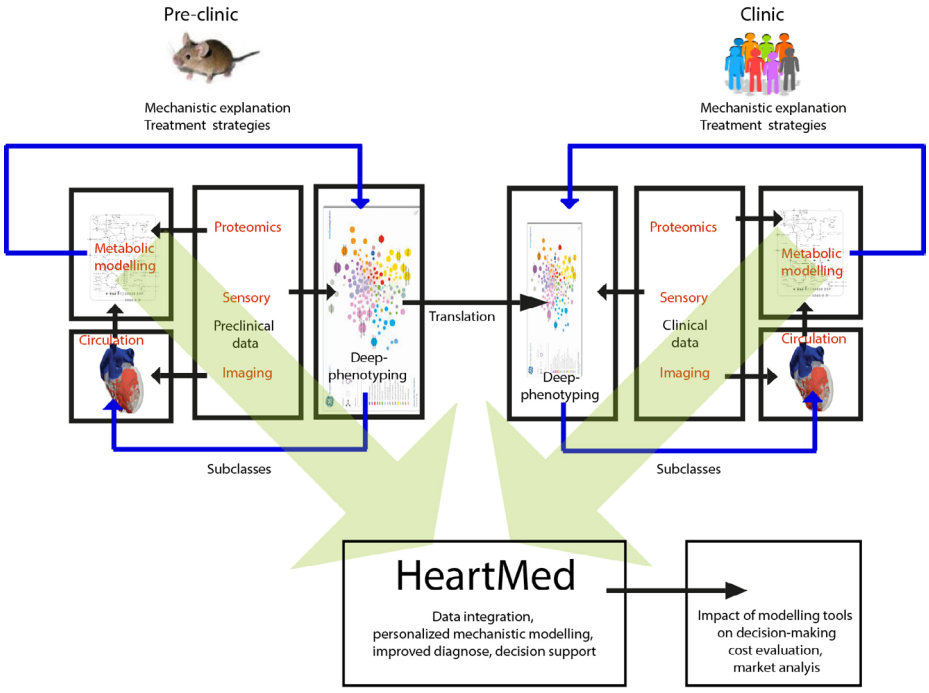
HeartMed

An ICT platform combining pre-clinical and clinical information for patient-specific modelling in cardiovascular medicine to improve diagnosis and help clinical decision-making

Heart failure is a complex heterogeneous clinical syndrome with several subclasses and the number one reason for death in the EU. Novel treatment strategies to better assess the needs of individual patients are currently being developed and some computational models have reached a level of maturity that makes them suitable for clinical use. However, patient-specific modelling relies on high quality input data that are difficult to obtain in clinical routine (missing data). Furthermore, some treatment strategies work in animal models of heart failure but fail in patients.
This project focuses on the handling of missing data and the interpretation of mechanistic differences between patients and animal models to enable personalised modelling for improved diagnosis in cardiovascular medicine. It will combine pre-clinical and clinical data, AI methods and mechanistic modelling into a novel concept – the HeartMed platform. The impact of the modelling tools on the decision-making processes will be investigated at the end of the project.

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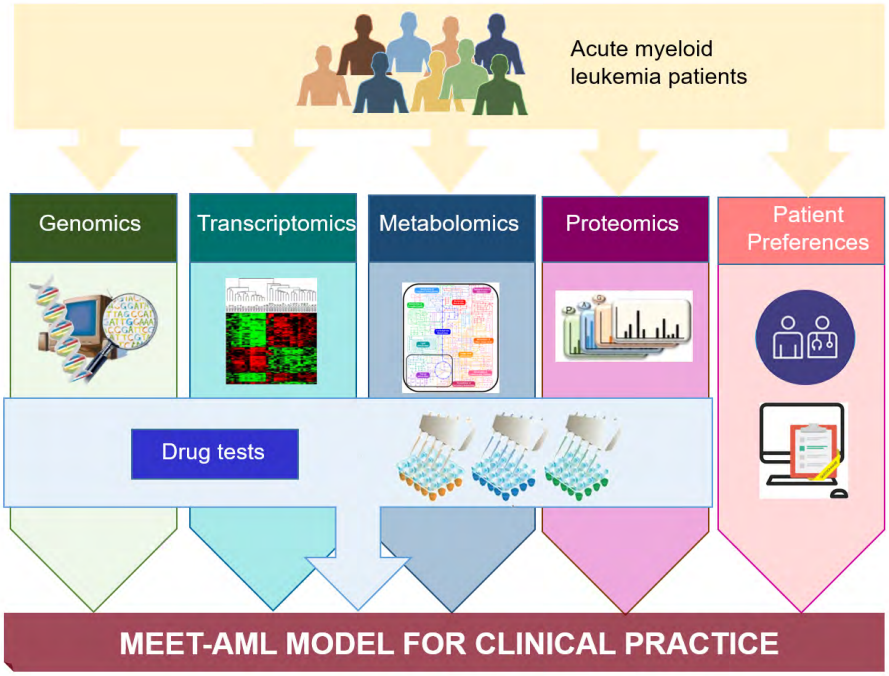
MEET-AML

Metabolic vulnerabilities for personalised therapeutic approaches in acute myeloid leukemia

Less than 30% of acute myeloid leukemia (AML) patients survive longer than 5 years. The metabolism of leukemic cells supports their production of energy and building blocks for growth and their capacity to resist to external attacks, as therapies. The study aims to identify metabolic activities of leukemic cells that lead to tumor cell death, once they have been switched off. This approach will combine genome and metabolism analysis, in order to identify and test, in the laboratory, personalised therapies. Moreover, the study will capture AML patients' preferences towards benefits and risks associated with different treatment options as well as their perspective towards this personalised approach. The study results will converge to a new model of personalised medicine in AML, meaning a new model of approaching the patient and taking decisions on his/her therapeutic path, based on his/her specificities, as patient and as human being and on direct patient involvement.



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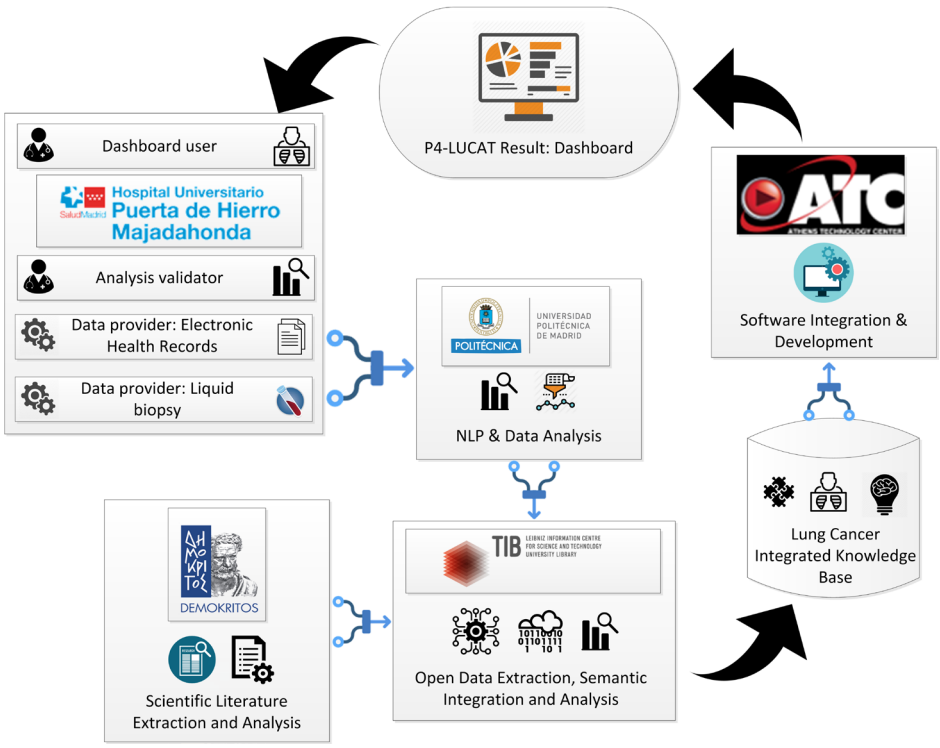
P4-LUCAT

Personalised medicine for lung cancer treatment: using Big Data-driven approaches for decision support

In the last decade, a wide range of new treatments have been proposed to heal lung cancer, the leading cause of cancer-related death in the world and its most frequent type. Still, the response to these new options strongly varies between patients, and few guidelines are available on how to optimise the treatment choice. P4-LUCAT proposes to address this issue by developing a technological solution supporting oncologists in the selection of the most appropriate lung cancer treatment. The project will develop a Big Data analytics dashboard, integrating patient data, public repositories and literature evidence. Such a tool will provide the practitioner with information about: (a) the efficacy of a treatment, tailored to the geno- and phenotypical characteristics of the patient; (b) the expected adverse effects and toxicities; and (c) relevant literature supporting these findings. This can only be achieved by integrating different sources of information, including Electronic Health Records, laboratory test results from liquid biopsies, scientific literature, and open structured data.

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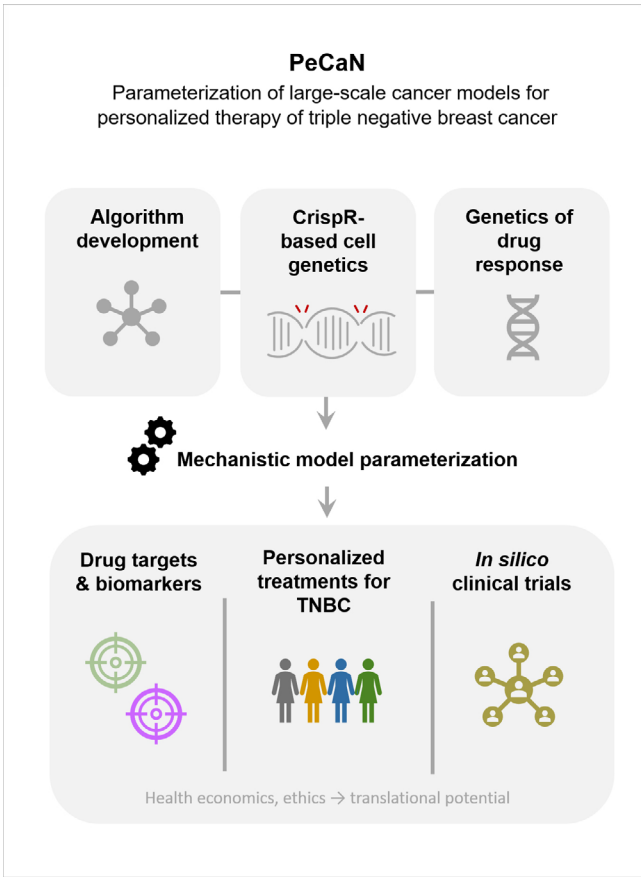
PeCaN

Parameterisation of large scale cancer models for personalised therapy of triple negative breast cancer

Triple negative breast cancers (TNBC) are an aggressive group of breast cancers, with high rates of relapse, poor survival outcomes and limited treatment options. Finding effective personalised treatment options is a critical unmet medical need. PeCaN aims to tackle this challenge through the development of advanced computational models for predicting individualised responses to targeted treatments, based on a deep molecular analysis of the patient and their tumor. In particular, we focus on solving the currently most difficult problem in model development: identifying the regions of the computational model parameter space that lead to the most accurate predictions. For this, we combine novel parameter optimization approaches, artificial intelligence, CRISPR-based cell genetics and single cell omics to generate parameterized models that can be used to predict patient-specific therapy responses and identify new drug targets and biomarkers. Candidates and predictions will be evaluated clinically, potentially providing real world evidence for their utility and offering a strong foundation for the development of future clinical trials.

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PerBrain

A Multimodal Approach to Personalised Tracking of Evolving State-Of-Consciousness in Brain-Injured Patients

Diagnosis of disorders of consciousness (DoC) patients cannot be misleading, as it guides critical decisions. Despite this importance current behavioral diagnosis often fails, in most cases due to the patients' major sensory and motor deficits. The need for accurate diagnosis and prognosis transcends patients: caregiving in DoC is very stressful, principally for the large uncertainty associated with them. The PerBrain Project will combine the multidisciplinary partners' expertise, and multisite and multimodal assessments of patients. Based on the collected data we will use state-of-the-art computational tools to develop a multimodal personalised diagnostic and prognostic tool for DoC patients. The overall aim of this project is to pave the way towards a better understanding of the pathophysiological mechanisms in DoC, which will, in turn, allow personalised rehabilitation strategies, and improved single-patient predictions of clinical state and prognosis.

DoC patient evolution	Multimodal layers	Patient's assessment
Acute phase	GCS; standard EEG + SEPs High density EEG Physiologic parameters (WP2)	Study of EEG patterns and primary sensory responsiveness
Subacute phase	CRS-R High density EEG ERPs TMS-EEG MRI, fMRI and DTI Physiologic parameters (WP2)	1) Evaluation of residual sensory, cognitive abilities and lesional load; 2) Evaluation of probability of consciousness 3) Measurement of complexity and its neural correlates
Chronic phase	CRS-R High density EEG ERPs TMS-EEG MRI, fMRI and DTI Physiologic parameters (WP2)	1) Follow-up evaluation of probability of consciousness; 2) Follow-up measurement of complexity and physiopathological correlates

A multi-layer hierarchical workflow for patients' evaluation


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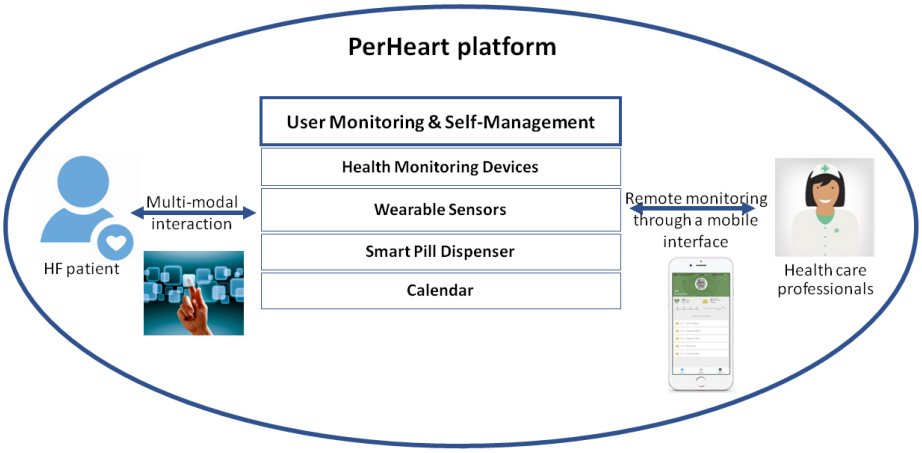
PerHeart

Personalised ICT solution to reduce re-hospitalization rates in heart failure elderly patients suffering from comorbidies

Heart failure is a major medical problem for which 1–2% of the health care budget is spent worldwide. It affects especially elderly, with 80% hospitalisations occurring among patients above 65 years. In addition, 70% of these patients are readmitted to hospital within one year, making re-hospitalisation an ongoing medical challenge. In this context, the PerHeart project is employing Information and Communication Technology with the main goal of reducing re-hospitalisation rates in heart failure patients by: supporting disease self-management; providing real-time personalised feedback for patients and their caregivers; elucidating specific risk factors for readmission; providing data that can help interpretation and prediction of complex multifactorial diseases. Transnational collaboration between multidisciplinary teams from five countries, combined with previous experience in developing ambient assistive living solutions, will ensure a successful implementation of the project.

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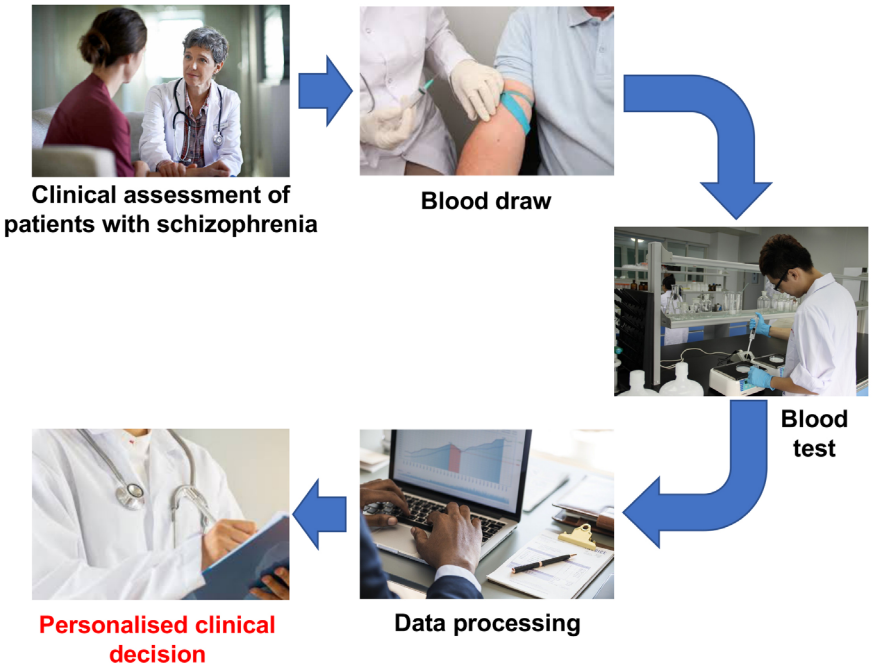
PerMedSchiz

Personalised medicine in schizophrenia: predicting relapse, treatment response and the potential benefit of add-on anti-inflammatory agents

Schizophrenia is a disabling mental illness that affects millions of Europeans. While antipsychotics alleviate symptoms in one-third of patients, the others are partially or completely refractory to treatment. Although guidelines are available, there is an urgent need to identify objective predictors of treatment outcome to guide personalised treatment. In this project, we will use advanced mathematical methods to analyse clinical and biological data that have been collected during the course of previous studies. We will generate blood-based clinical decision support systems to identify patients at risk of non-responding to conventional antipsychotic monotherapy, patients at risk of relapse following treatment, and patients at risk of developing antipsychotic-induced adverse effects. We will also conduct a placebo-controlled clinical study to assess the efficacy of a new therapeutic protocol and to model its cost-effectiveness when combined with a blood test for selecting patients.

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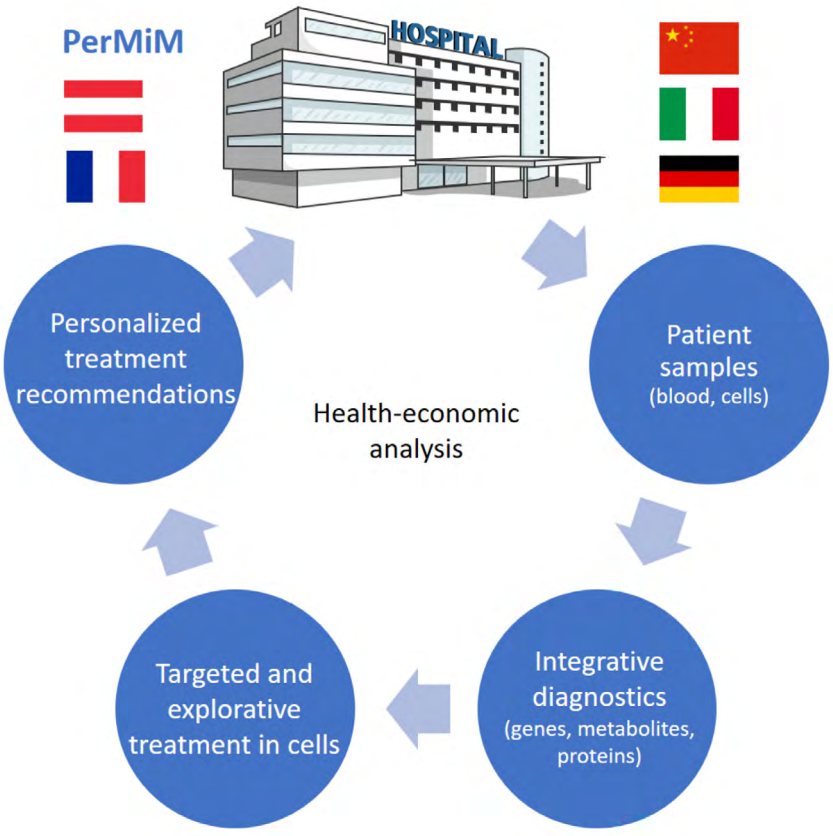
PerMiM

Personalised Mitochondrial Medicine: Optimizing diagnostics and treatment for patients with mitochondrial diseases

There are more than 1,000 metabolic disorders among which a large fraction affects energy metabolism in mitochondria, the powerhouses of our cells. Several mitochondrial disorders are amenable to treatment, often with a simple diet change such as vitamin supplementation. However, pinpointing the genetic cause of mitochondrial disorders and determining the appropriate treatment remains open for most affected individuals. To address this challenge, the Eurasian personalised mitochondrial medicine project (PerMiM) aims for early diagnosis by integrating information on the patient's genes, metabolites, and proteins. Early diagnosis guides the patient's management and defines personalised treatments targeted to their individual need. Moreover, where the disease cause is still unclear, we will characterize the molecular response of patient cells to various treatments and translate these results into advanced clinical management. In parallel, health-economic analysis of this multi-centre project will contribute to improved evidence-based best practice.

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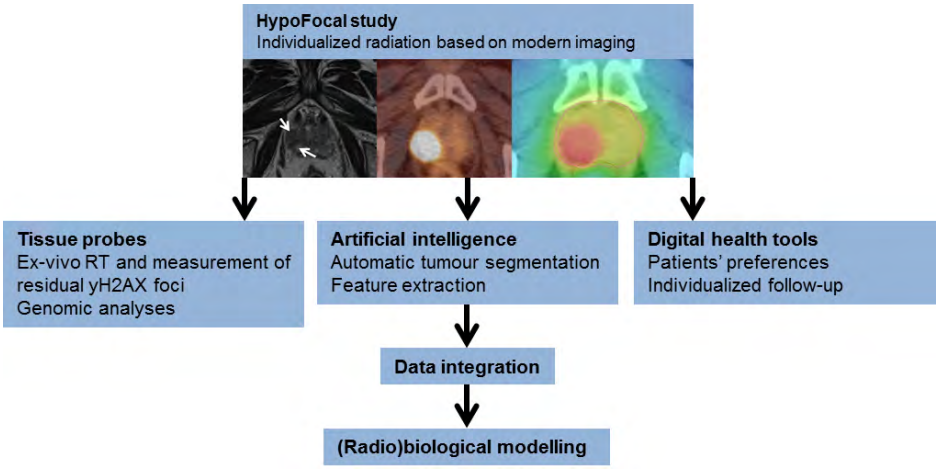
PersoRad

Implementation of mobile health tools and artificial intelligence for personalised radiation treatment planning and monitoring in prostate cancer

Prostate cancer (PCa) is the most frequent diagnosed malignancy in male patients and radiation therapy (RT) is a main treatment option. However, RT concepts for PCa have an imminent need to be rectified in order to personalise the RT strategy by considering (i) the individual PCa biology and (ii) the individual disease process of each patient. The consortium concatenates a prospective, nonrandomized phase II trial for personalised RT of PCa patients (HypoFocal) with novel tools for patient involvement, advanced "omic" and bioinformatical analyses. Hereby, the implementation of novel computational components enables (i) unbiased characterization of tumor and normal tissue biology for personalised treatment planning processes (ii) direct integration of patients' preferences for a personalised treatment planning and follow-up process after RT.

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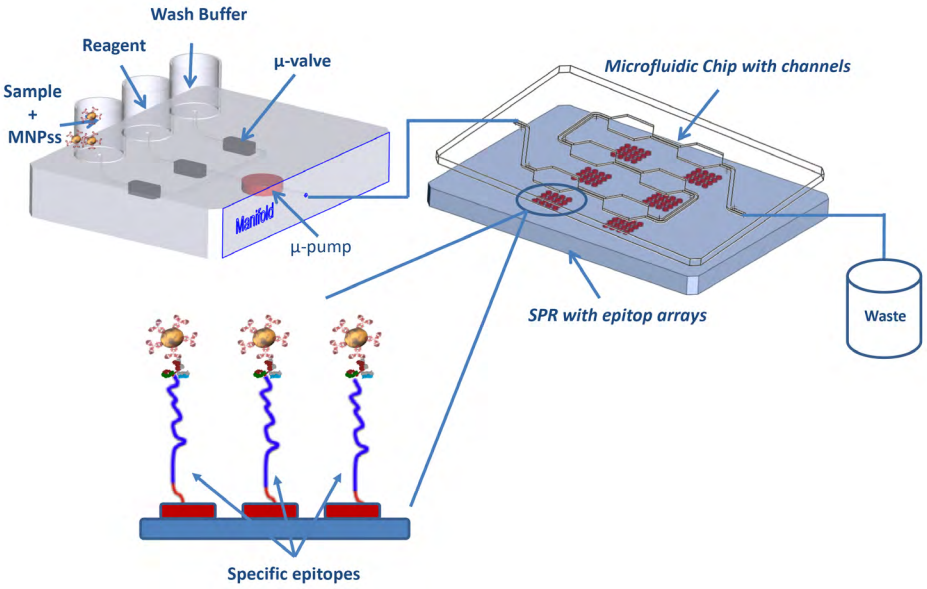
POC4Allergies

Point-of-Care system for personalised diagnosis and assessment of treatment efficacy for allergies

Allergy is the most common chronic disease in Europe - more than 150 million Europeans suffer from chronic allergic diseases and the current prediction is that by 2025 half of the entire EU population will be affected. Up to 20% of patients with allergies live with a severe debilitating form of their condition, struggling with the fear of a possible asthma attack, anaphylactic shock, or even death from an allergic reaction.
The aim of the project is to develop a POC analytical platform for a more precise and predictive personalised diagnosis of allergies, supporting personalised diagnostics and treatment monitoring. Aiming at hazelnut and peanut allergies, we are tackling two of the most threatening and frequent food allergens. The study will develop a less invasive and burdening diagnosis tool for allergy, allowing early recognition and improving quality of care for patients.

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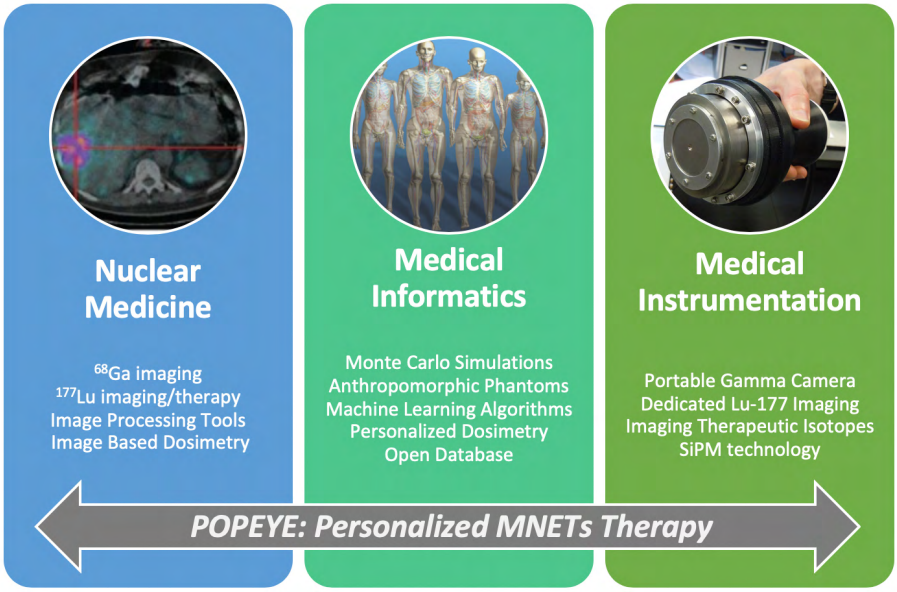
Popeye

Personalised Optimization of Prognostic and thErapeutic protocols with Lu-177 for MNETs, with the development of advanced computational tools and a portable detection sYstEm

It is overall estimated that more than 12,000 people in the USA are diagnosed with a neuroendocrine tumor (NET) each year. POPEYE project uses advanced computational tools for the optimization of midgut MNETs treatment, towards the personalisation of ^{177}Lu-DOTA-peptide therapeutic protocols. An interdisciplinary approach exploits established tools and novel developments to increase the early, effective diagnosis, and the efficacy of ^{177}Lu-DOTA-peptide radionuclide therapy. Clinical data are used to optimize the quantification on SPECT/PET acquisitions and accurately extract tumor radiomics. Monte Carlo simulations, incorporating Machine Learning techniques, serve as gold standard and allow dosimetry estimation on personalised treatment protocols. POPEYE's ultimate goal is the clinical evaluation and exploitation of the proposed software & hardware tools to assess personalised MNETS diagnosis and therapy protocols. The multidisciplinary experience of the consortium members (Greece, France, Austria) ensures the efficient implementation of the project.



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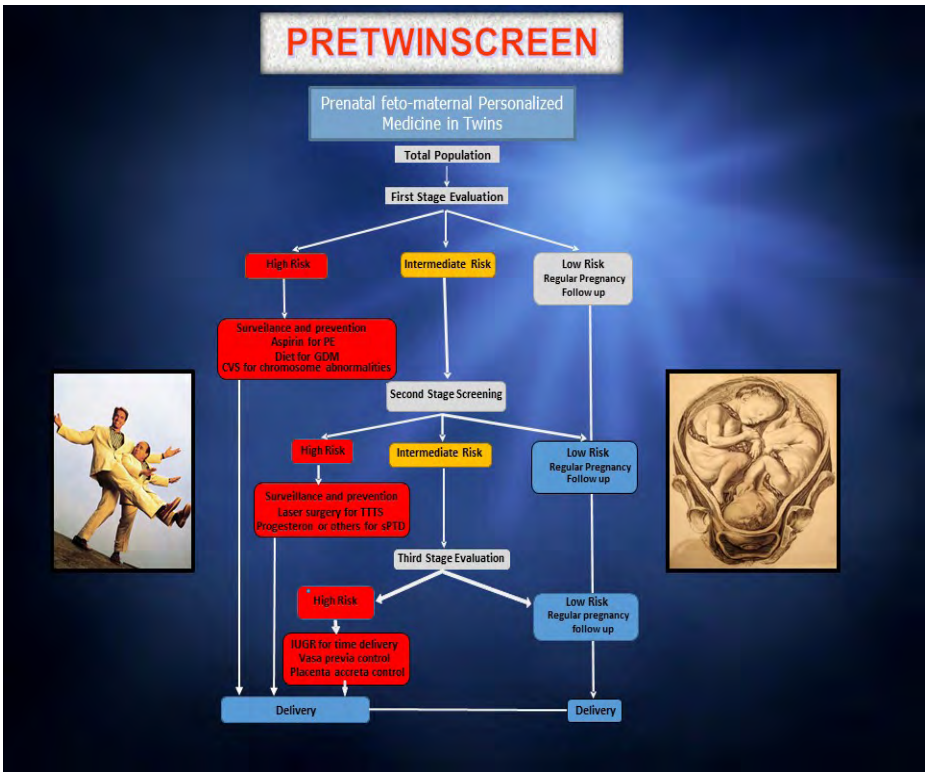
PRETWINSCREEN

Develop a multi-disciplinary approach for a personalised prenatal diagnostics and care for twin pregnancies

Prevalence of twin pregnancies is rising globally due to increased assisted conception and advanced maternal age in pregnancy. Twins have 5-9 higher prevalence of major pregnancy complications such as prematurity, low birth weight, pregnancy hypertension and diabetes. They also have special syndromes of identical twins. Consequently, more twins are born prematurely, suffer from low birth weight, cerebral palsy, etc., often requiring admission to newborn intensive care units, and develop motor and cognitive disorders for life. These impose a huge burden on individuals, families, and the society. Our group will develop special methods for prediction and prevention of pregnancy complications in twins, and conduct modelling with our large study size. With multiple measures we will yield a comprehensive way for identifying twin risks, offering personalised, preventive clinical care of their disorders. This would enable a paradigm shift in prenatal personalised care for twin pregnancy.



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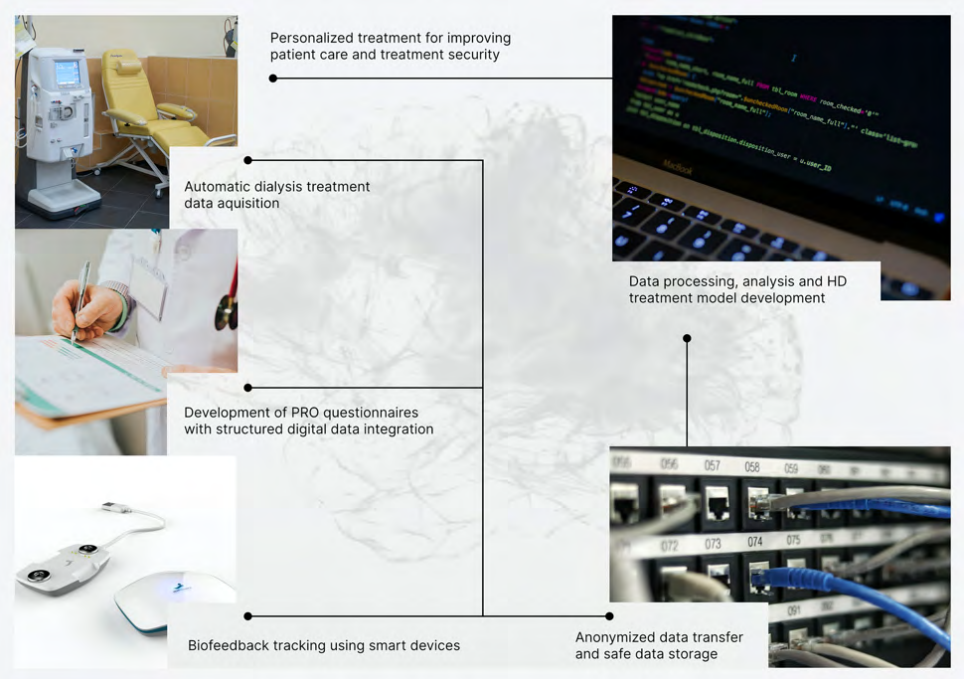
ProDial

Patient-Reported Outcome, Biodata and Process Data to Evaluate Dialysis Tolerability

Haemodialysis (HD) treatment affects around 0.1% of the population but requires 5 to 10% of overall health costs in developed countries due to complex and chronic patient care. Since quality and process control of HD treatment is nowadays not based on an assessment of patient-specific biochemical and procedural dialysis measures, the ProDial project aims at developing an individual approach based on the granular characterization of the patients' surrogate biodata of sympathetic activation following HD treatment, physical activity, sleep quality, recovery time, self-reported tolerability outcome and HD machine data with the goal to increase individual treatment outcome and tolerability. Innovative and anonymised data gathering and validation procedures will assure integrated and structured data storages while innovative mechanisms will analyse the contained data to enable personalised HD treatment procedures with intelligent comorbidity and tolerability adaptation in the future.

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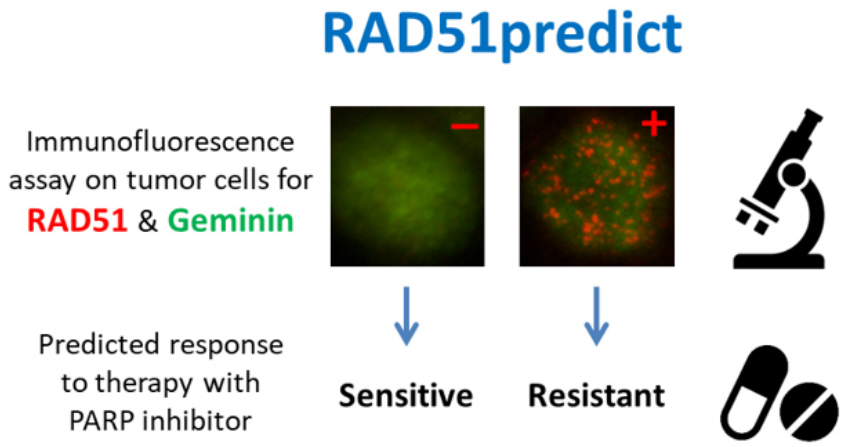
RAD51predict

Patient stratification based on DNA repair functionality for cancer precision medicine

Tumours with DNA repair defects, such as those from BRCA1/BRCA2-mutation carriers, respond very well to certain chemotherapies and to new targeted drugs named PARP inhibitors (PARPi). We have developed a new test based on the visualisation of a DNA repair protein named RAD51 that enables to establish if tumour cells have DNA repair defects, beyond mutations in BRCA1/BRCA2. This project aims to establish the predictive value of the RAD51 test in four major cancers types (breast, ovarian, prostate and endometrial) and if the test provides functional evidence for the interpretation of genetic variants of unknown significance. In addition, we will improve the test to enable its implementation in the clinic and perform an economic evaluation to compare our test versus current selection criteria for PARPi therapeutic indications.

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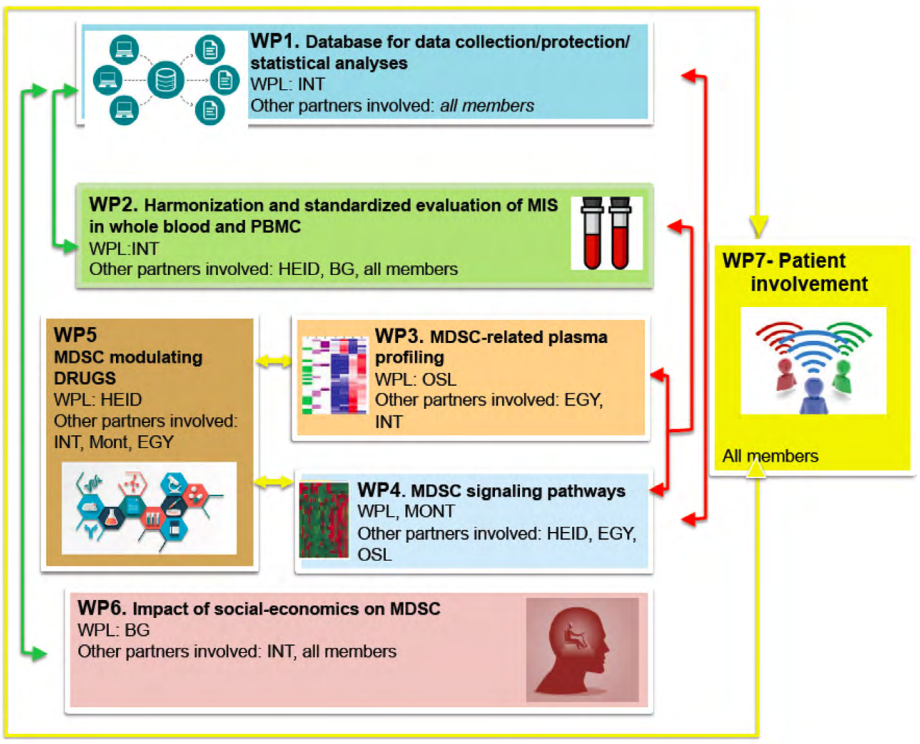
SERPENTINE

Quantifying systemic immunosuppression to personalise cancer therapy

Controlling cancer by medical treatment depends on the tumor nature but also on the ability of our immune system to recognize and control tumor growth. We identified one important mechanism used by tumor to weaken immune defense involving a particular type of immunosuppressive cells (the myeloid cells), and most importantly we have found a test (the Myeloid Index Score, or MIS) to measure this weakness by a simple blood analysis. In the Serpentine proposal, thanks to the join-effort of different cancer centres in Europe and abroad, we are committed to prove that MIS might help individualize those cancer patients whose immune system suffers of such a weakness and to demonstrate that these patients would need more intensive treatment regimens to obtain disease control. We are also going to study and possibly discover strategies to counteract myeloid-mediated immunosuppression in order to help improving cancer therapy at patient-tailored level.

The SERPENTINE Project – WP flow

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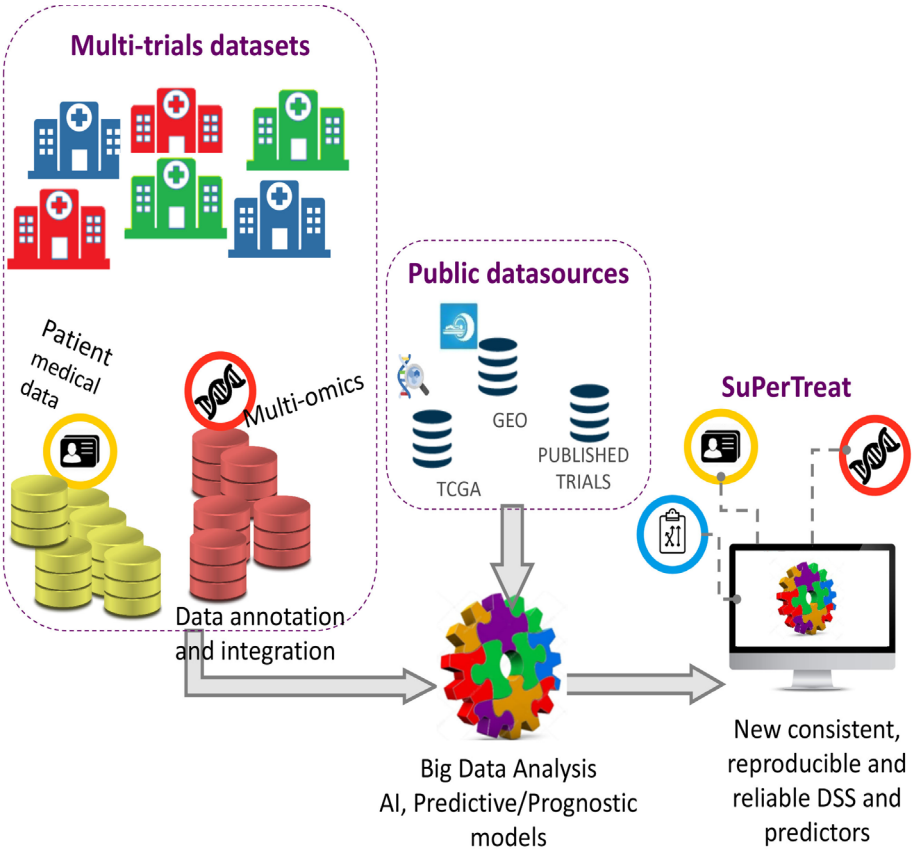
SuPerTreat

Supporting Personalised Treatment Decisions in Head and Neck Cancer through Big Data

Head and Neck Cancer (HNC) is a deadly disease affecting more than 630.000 patients each year in the EU. Treatments may be extremely impairing with hard impacts on aesthetics, swallowing, breathing and patients' quality of life. HNC presents extremely different biological characteristics, which would significantly benefit from personalised patients' classification and personalised treatment. Despite significant advances in therapies, at present treatment decisions are taken on a "one size fits all" approach, based on few clinical and risk factors, the so-called TNM system, as no biomolecular predictors of disease outcome are yet validated. Using AI and advanced modelling techniques, SuPerTreat will analyse the different biomolecular characteristics of HNC that discriminate patients into high/medium/low-risk subgroups in the aim to identify how combined clinical, lifestyle and biomolecular factors concur to response to treatments, recurrence and survival. The so generated knowledge will inform personalised treatment.

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TRAJECTOME

Temporal disease map based stratification of depression-related multimorbidities: towards quantitative investigations of patient trajectories and predictions of multi-target drug candidates

Depression is a commonly occurring mental disorder that usually have a chronic recurrent course throughout the life causing extensive sufferings to the patients. Previous studies suggest that depressed patients are prone to develop several other disorders, so called multimorbidities, most likely due to common biological and environmental risk factors. The aim of the TRAJECTOME project is to investigate how these multimorbidities emerge in time in order to identify disease trajectories. These disease trajectories will help to distinguish depressed patients with similar multimorbidity profiles and identify which specific biological, socioeconomic and lifestyle factors contribute to the development of their symptoms. By understanding these processes, the TRAJECTOME project will enable improved disease prediction and prevention in depression and also provide new insight for drug discovery to promote personalised medicine in depression related multimorbidities.