ERA PerMed

NEWSLETTER 7

January 2022

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

ERA PerMed Results of the Joint Transnational Call 2021

Multidisciplinary research projects on personalised medicine – development of clinical support tools for personalised medicine implementation

22 successful consortia are funded with a total investment of approximately 27 million Euros for three years

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ERA PerMed 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.

Looking back at 2021 and into the future

These past years have taught us all many important lessons in patience, flexibility, adaptability and resilience. While everyone hoped that 2021 would be free of the negative impact and impediment of the Covid-19 worldwide pandemic, we at ERA PerMed, did not let the circumstances hold us back. In this past year, 2021, we have executed our 4th call for proposals, JTC2021, of which you can read about in more details in this newsletter. We have collaborated with ICPerMed on preparing the draft document for the future European Partnership for Personalised Medicine (EP PerMed), as well as an open information day in May on the topic, and recently, we announced a 5th call for proposals, JTC2022, which is now open for applications!

ERA PerMed strides to play a key role in the European personalised medicine ecosystem, and to further expand its influence and international impact by reaching out and connecting with funding organisations and other stakeholders around the globe with the goal of promoting multi-national, collaborative research in all aspects of personalised medicine worldwide.

With this, we wish you all good health, brilliant and innovative research, fruitful and rewarding collaborations and meaningful progress in promoting personalised medicine worldwide this New Year 2022!

ERA PerMed Joint Transnational Call 2022!

"PREVENTION IN PERSONALISED MEDICINE"

Submission deadline for preproposals: February 17th, 2022
Click for details

Recordings of the Information Event on the Call can be found *here*

Open for Applications!

ICPerMed "Best Practice in Personalised Medicine" Recognition 2021

Deadline: January 28th, 2022
Click for details

HAVE A LOOK AT OUR PREVIOUSLY FUNDED PROJECTS
here

Joint Transnational Call for Proposals 2021:
"MULTIDISCIPLINARY RESEARCH PROJECTS ON PERSONALISED MEDICINE – DEVELOPMENT OF CLINICAL SUPPORT TOOLS FOR PERSONALISED MEDICINE 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, 30 funding organisations (FOs) from 23 countries agreed to launch the fourth ERA PerMed Joint Transnational Call 2021 (JTC2021) for collaborative innovative research projects in PM. With the JTC2021 on "Multidisciplinary Research Projects on Personalised Medicine – Development of Clinical Support Tools for Personalised Medicine Implementation", ERA PerMed aimed to promote innovative interdisciplinary collaboration and to encourage translational research projects by building 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.

Two new funding organisations, which were not part of previous ERA PerMed Calls, joined the JTC2021: Brazilian National Council of State Funding Agencies (CONFAP) from Brasil and Agencia Nacional de Investigación y Desarrollo (ANID) from Chile. The joining of these two new funding agencies to the call represents ERA PerMed's strive for global collaboration in the field of PM.

217 eligible pre-proposals were submitted, 59 consortia were invited to submit a full-proposal and **22 consortia with a total funding amount of 26,776,871€** will be funded!

One of the main objectives of all ERA PerMed calls is to support outstanding translational and **transnational** research projects in the field of PM. In line with the transnationality objective, we are happy to report that out of the 30 FOs supporting the JTC2021, 27 are successfully involved in the funding of the 22 successful projects. This wide involvement of countries was also thanks to the widening process, which allowed the consortia to include a new project partner from a FO that was underrepresented in the first stage of the call, in the full proposal phase.

The topics of the excellent projects that were selected for funding include a broad range of different diseases, such as cancer (endometrial, gastric, lung, pancreatic cancer, lymphoma, cachexia linked cancer); renal diseases (nephrotic syndrome, renal transplantation); cardiovascular diseases, acute circulatory failure, preeclampsia and gestational hypertension; chronic obstructive pulmonary diseases; Neurological diseases (neurodevelopmental disorders, dementia prevention strategy, depression, Alzheimer's disease, behavior disorders) ; rheumatoid arthritis and systemic auto-inflammatory diseases. You can read more about the various topics, the objectives and the researchers involved in the successful consortia in the following pages.

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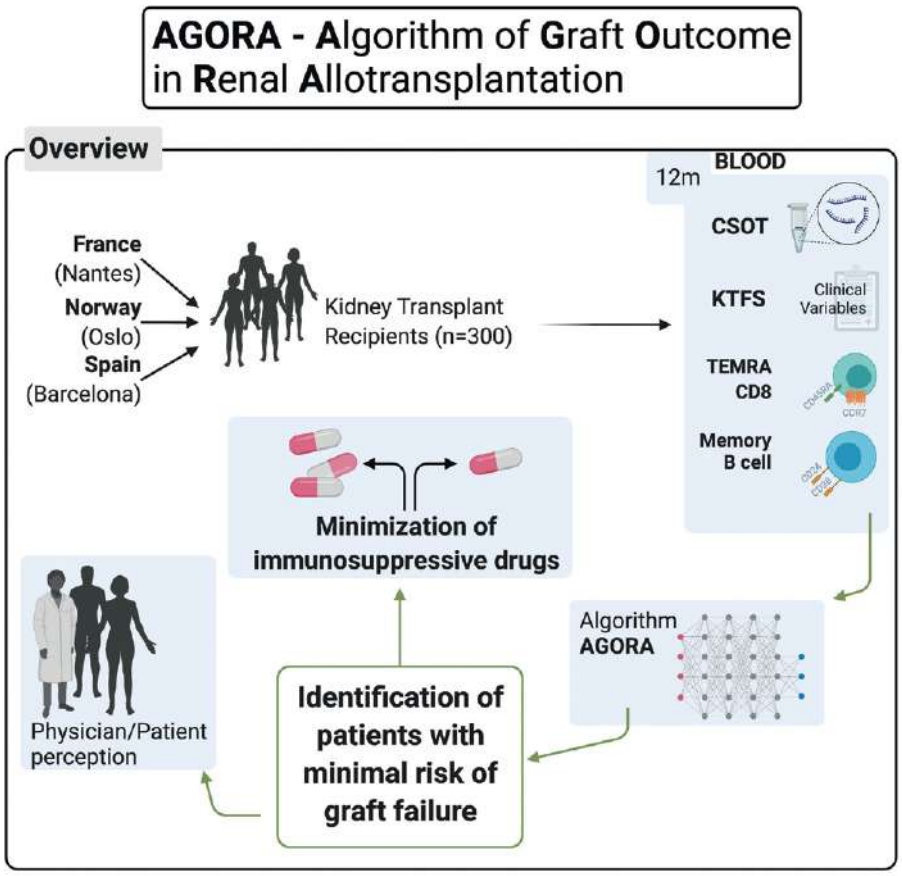
AGORA

Algorithm of graft outcome in renal allotransplantation

In renal transplantation, monitoring the risk of subclinical rejection and graft failure remains challenging. AGORA partners developed and validated non-invasive biomarkers allowing the prediction of patients at high/low risk of subclinical rejection and graft failure. The objectives are to build a European non-invasive clinical decision-making tool for immunological risk stratification of graft failure through a retrospective study on an existing biocollection of 300 patients and a multicenter randomised open label trial of immunosuppression minimisation AGORAC. Economic efficiency will be evaluated during the trial. We will integrate users' perspectives by performing sociological interviews to promote the involvement of patients in their clinical care and to help clinicians in decision-making. Ancillary functional studies will reinforce AGORA to assess immunological events following immunosuppression minimisation. AGORA could impact the health care pathway for kidney transplant recipients by incorporating a medical decision tool for personalising immunosuppressive therapy.

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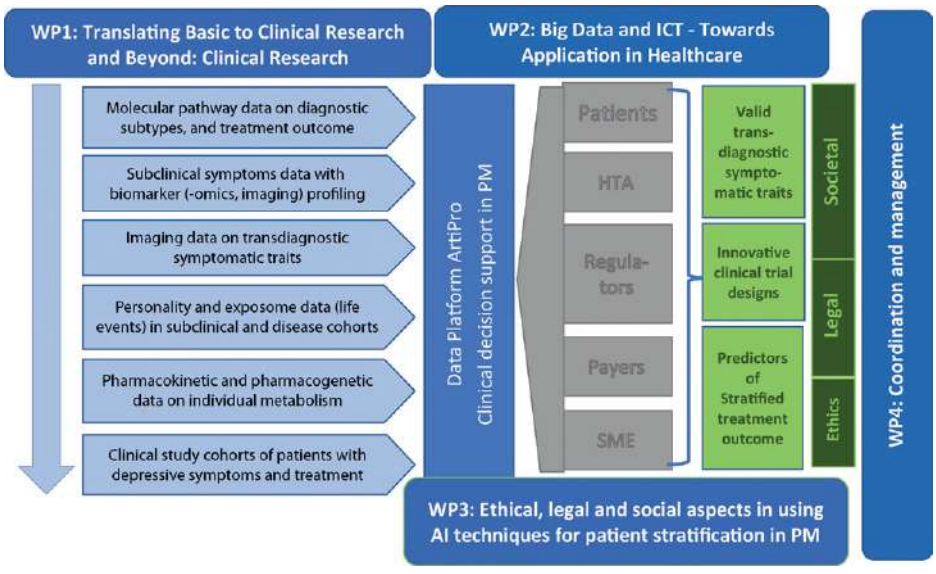
Artipro

Artificial intelligence for personalised medicine in depression - analysis and harmonisation of clinical research data for robust multimodal patient profiling for the prediction of therapy outcome

Personalised medicine aims to predict therapeutic response according to a personal profile that includes clinical, biological, and genetic data. This project focuses on depression. It aims to establish an artificial intelligence platform that brings together data from clinical research on the components of these profiles with the purpose of identifying predictors for response to depression treatment. The results will be combined into a single data platform that enables the use of large multimodal datasets to develop predictive models of symptoms and outcome data, thus enhancing the impact of these data. Artificial intelligence approaches will be investigated to identify novel biomarkers that can predict response to treatment. This will help to develop of a decision support system for personalised therapy while identifying the specific ethical and legal requirements that need to be fulfilled.



The Artipro project will take advantage of the use of biomarker data obtained from clinical research and perform an AI based analysis of multimodal biomarker profiles for the benefits on health care personalisation and regulatory decisions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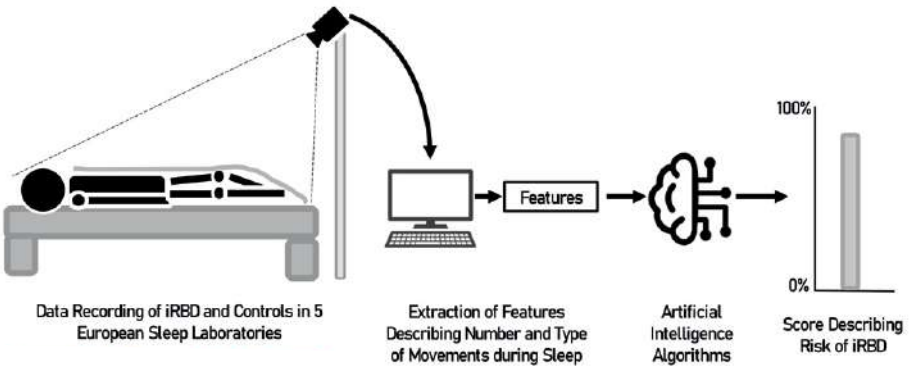
BRAVA

Behaviours in REM sleep: personalised automatic 3D video analysis as novel tool to detect alphasynucleinopathies

Rapid eye movement (REM) sleep behaviour disorder (RBD) is characterised by abnormal muscular activity and dream enactment in REM sleep. In its isolated form (iRBD), it is recognised as an early stage of alpha-synucleinopathies (i.e. Parkinson's disease, dementia with Lewy bodies and multiple system atrophy). However, iRBD is often not recognised. An early, accurate, automated and population-extended recognition of iRBD, would be essential to recognise patients in early stages of alpha-synucleinopathies, enabling a timely initiation of disease modifying treatments. Furthermore, objective and automated methods would improve follow up of iRBD patients and allow personalised treatments. We aim to develop and validate a novel small, light and portable 3D video-based technology employing artificial intelligence as powerful, automatic, stand-alone instrument to identify and follow-up iRBD patients. We believe that this novel tool can revolutionise the way in which iRBD patients are identified and followed-up.



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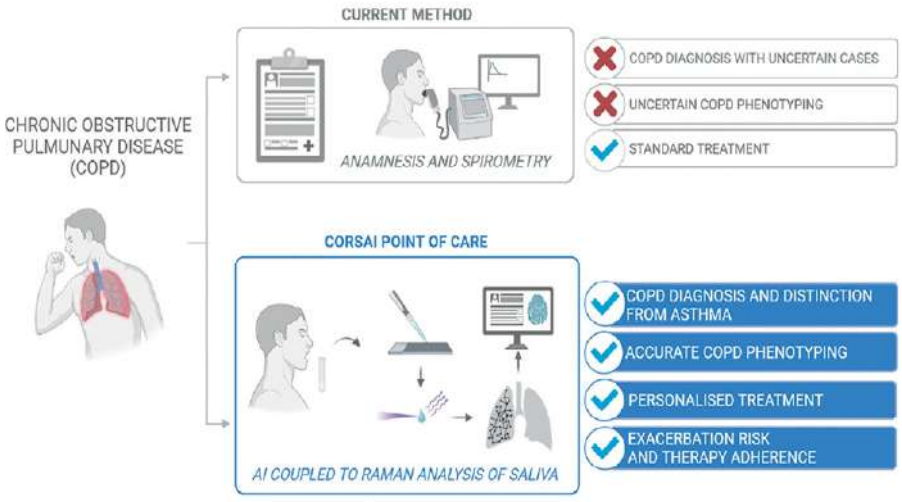
CORSAI

Raman analysis of saliva from COPD patients as new biomarker: AI-based point-of-care for the disease monitoring and management

Chronic obstructive pulmonary disease (COPD) is a debilitating and chronic pulmonary syndrome that causes a rapid decline in lung function. Nowadays, there is not specific biomarker that allows its immediate identification and the phenotyping of COPD patients is based on very long standard procedures, exposing them to the high risk of exacerbation and hospitalisation. Therefore, it is of primary importance to search for a unique biomarker that can help clinicians in the differential diagnosis of COPD patients from those with asthma, the evaluation of their exacerbation risk and the identification of non-adherence to therapy. On the basis of this, the main goal of the CORSAI project is to validate a new method based on the Raman spectroscopy (RS) analysis of saliva (ideal biofluid for diagnostics and monitoring purposes, as the collection procedure is minimally invasive) for the optimised and personalised management of COPD patients. The Raman spectrum of saliva (Raman fingerprint) will represent a single biomarker for COPD, obtained in a sensitive, fast and label-free manner. By the combination of RS-based method with artificial intelligence (AI), the project will lead to the COPD patients' management in a personalised medicine dimension, with a particular focus on stratification of patients, prediction of the risk of exacerbation and adherence to therapy. Finally, the ultimate goal is to transfer the RS directly to the hospital, thanks to the use of a portable Raman spectroscope: it will be possible to test the effectiveness of a point of care method able to investigate different aspects of COPD in a single analysis.

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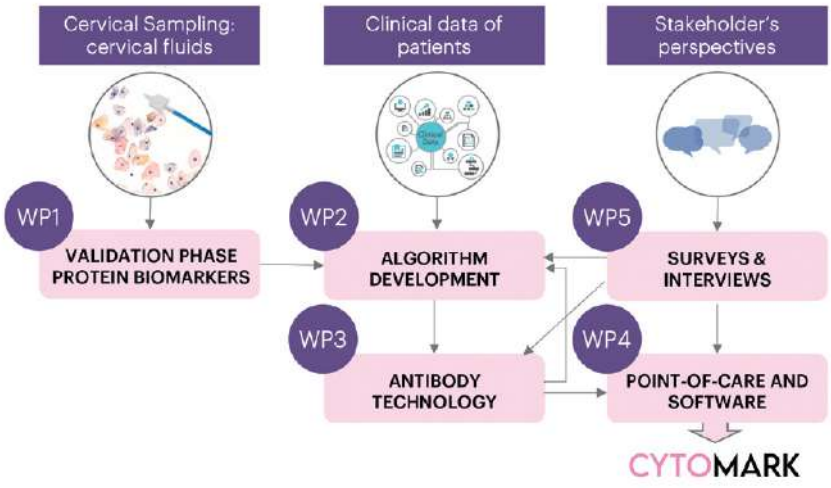
CytoMARK

Development of a personalised non-invasive diagnosis of endometrial cancer using proteomic markers in cervical fluids and clinical data

Endometrial cancer is the fourth most common cancer in women, and its incidence is increasing. Early detection is fundamental to patients' survival. Currently, no screening methods are available and diagnosis is a multistep process that includes minimally-invasive and invasive tests. **This inaccurate diagnostic process is a burden on our healthcare system**.

This funded project aims is to **advance the development of a non-invasive, objective, and personalised diagnostic tool of endometrial cancer using cervical fluid protein biomarkers and clinical data**. In this proposal, we will validate protein biomarkers in a retrospective clinical study coordinated by VHIR (Spain) and with the top-edge technology on targeted proteomics, led by the LIH partner (Luxembourg). Molecular markers will be combined with clinical data by the USC partner (Spain) and the most promising biomarkers will be transferred to an antibody technology by ICOSAGEN (Estonian SME partner) and SolarBiotec (Turkey SME partner). Throughout the project, the HU partner (Turkey) and VHIR will ensure the clinical validation of the developed non-invasive tool and the valorisation of the asset to meet the stakeholders' requirements. The resulting tool is a **change in the paradigm** on how endometrial cancer patients are managed and will benefit patients, doctors and the health system.



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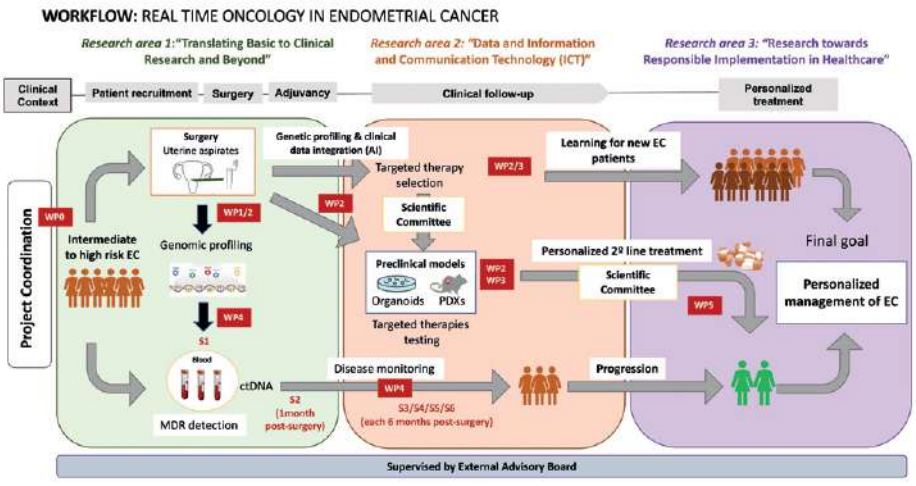
ECLAI

Personalised clinical management of Endometrial Cancer using Liquid biopsy, genomics and Artificial Intelligence

Precision oncology represents a challenge when it comes to Endometrial Cancer (EC). The incidence of this cancer has increased in the last years and the prognostic and therapeutic options for advanced disease stages are still poor. Thus, to improve the treatment of EC patients with poor prognosis, it is necessary to gain more knowledge in the cancer molecular biology and also in the new approaches to capture the innate intra-tumour heterogeneity (ITH), which is highly present in EC. The objective of the ECLAI consortium is to reach personalised EC management by developing new tools that recapitulate the heterogeneous molecular composition of tumours and finally establish new and effective therapeutic regimens. With this aim, our consortium will combine: a) the use of non-invasive biopsies, which capture ITH, and the genomic characterisation of the tumour within the disease evolution, b) the generation of preclinical models to test personalised alternative targeted therapies and c) the use of machine learning strategies to decipher a recurrence and therapeutic response rate algorithm, named ECLAI, with clinical application to improve EC management. This workflow will be applied with the advise and support of patients' associations and ENITEC, the European research network on EC. Altogether, this pioneering strategy has the final goal to improve the management and life quality of EC patients who currently have limited clinical opportunities.

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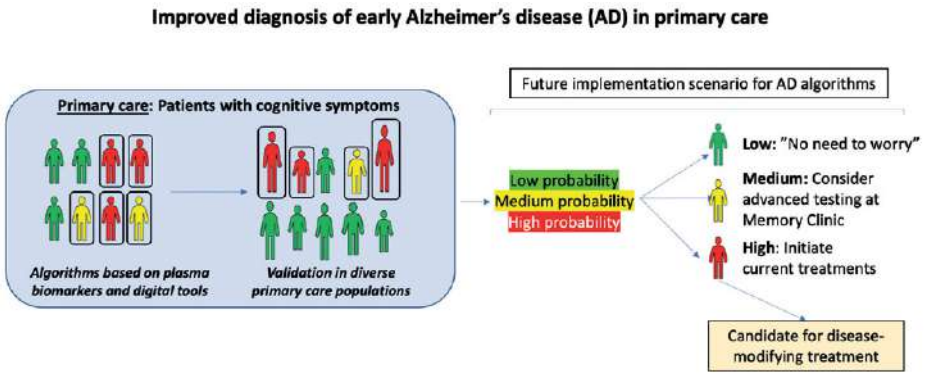
EDAP-AD

Early and accurate diagnostic and prognostic markers for Alzheimer's disease

Alzheimer's disease (AD) has a major impact on daily functioning and quality of life and is characterised by a huge socio-economic burden, with at least 50 million people affected worldwide. For clinical practice, we need to develop algorithms based on easily accessible and time- and cost-effective tests like blood-based biomarkers and digital cognitive tests for personalised diagnosis, prognosis and correct symptomatic treatment. For clinical trial development, we need to optimise the screening procedure to accurately identify individuals with AD in pre-symptomatic stage or prodromal disease stages and predict progression rates at an individual level. The methods need to be robust and generalizable, and the test results need to be optimally communicated to patients. This initiative will leverage demographically and ethnically diverse population-based, primary care and memory clinical cohorts that are deeply phenotyped and have long-term follow-up data available. Using state-of-the-art machine learning approaches, we will define, validate and implement accessible and cost-effective AD biomarkers for personalised diagnostic and prognostic work-up, and to facilitate development of disease modifying treatments in AD. By revolutionising the diagnostic work-up and improving participant selection and monitoring for clinical trials, the personalised medicine approach developed in EDAP-AD will meet the challenges posited by AD.



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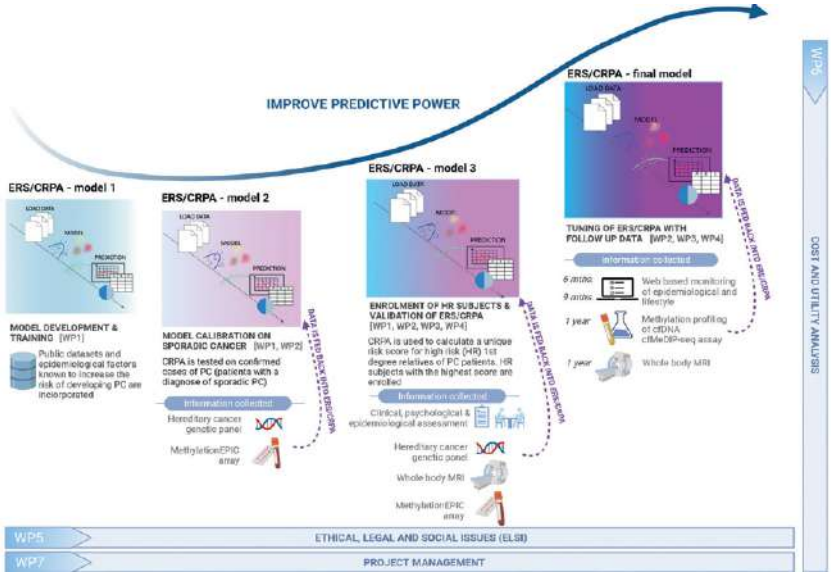
IMAGene

Epigenomic and machine learning models to predict pancreatic cancer: development of a new algorithm to integrate clinical, omics, DNA methylation biomarkers and environmental data for early detection of pancreatic cancer in high-risk individuals

Pancreatic cancer (PC) has the lowest survival rate of all cancers in Europe, with no early detection strategies available. First-degree relatives of patients with PC have at least a 2-fold increased risk of developing the disease, although it is well-known that besides family history, also older age, tobacco, alcohol abuse and other epidemiological risk factors predispose to PC onset. Even in families with high genetic predisposition to PC, existing cancer predictive Machine Learning models are of very limited use, since their predictive accuracy is generally low. Epigenetic biomarkers are not a part of existing risk indexes yet, although strong evidence shows that methylation patterns in blood can efficiently predict cancer mortality and that liquid biopsy has a potential to revolutionise early cancer diagnostics. The IMAGene project will develop, calibrate and test a comprehensive Cancer Risk Prediction Algorithm (CRPA) to predict PC in high-risk (HR) asymptomatic subjects, by including omics, imaging, epidemiologic, lifestyle and psychological data records. IMAGene will also investigate the potential for DNA methylation biomarkers to improve currently available risk indexes, and validate the feasibility of using liquid biopsies for early detection of cancer in HR individuals. A detailed ethical and cost-utility analysis will respectively guide a responsible application of the procedures and will balance benefits and impact for the health care system in four EU countries.



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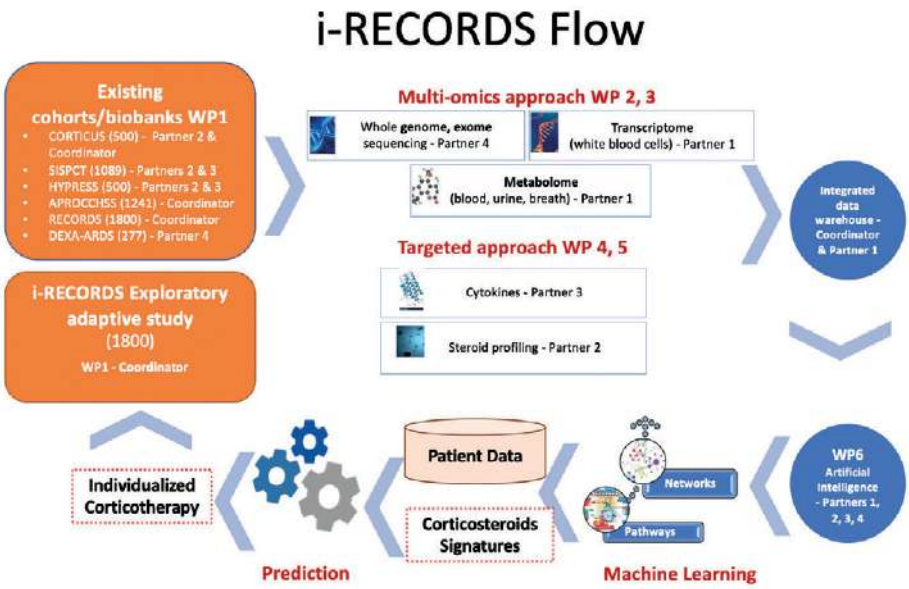
i-RECORDS

International – Rapid rEcognition of CORticosteroiDs sensitivity or resistance in Sepsis

Sepsis and COVID-19 are a major burden for populations worldwide. In sepsis/COVID-19, a dysregulated host response to infection is the hallmark supporting the routine use of corticosteroids (CS), a low-cost and highly efficient class of immunomodulators. Stratifying patients based on individual immune response may improve the balance of benefit-to-risk of CS treatment.

iRECORDS will generate signatures of CS sensitivity/resistance of individual septic/COVID-19 patients. These signatures will be based on characterisations of biological systems by using targeted approaches at levels of DNA, RNA, proteins (i.e. cytokines), hormones, and metabolites. We will use Artificial Intelligence methods to develop efficient signatures by integrating the high dimensional multi-level data from previous studies and newly generated data. The resulting signatures will define personalised treatment rules for patients, and thereby improve their chance to survive.



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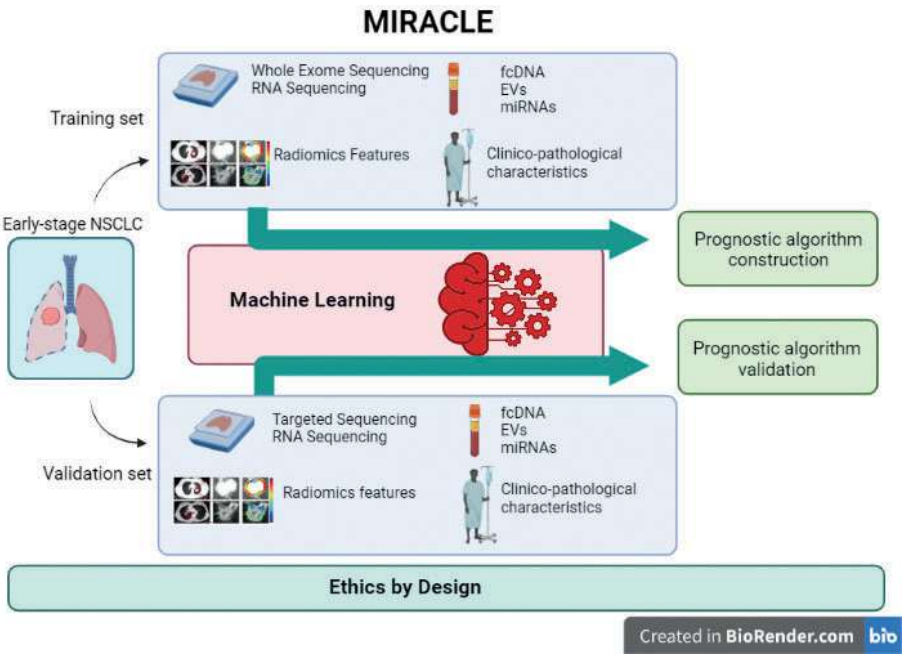
MIRACLE

A machine learning approach to identify patients with resected non-small-cell lung cancer with high risk of relapse

Early-stage non-small-cell lung cancer (ES-NSCLC) represents 20-30% of all NSCLC and is characterised by a high survival rate after surgery, with variability in clinical outcome among patients sharing the same disease stage, suggesting that other factors could determine the risk of relapse. We hypothesize that multiple factors could influence the prognosis of resected ES-NSCLC patients, such as tumour tissue and tumour microenvironment (TME) characteristics, liquid biopsy, radiomics features and clinical-pathological factors. MIRACLE aims to develop and validate a machine learning algorithm acting as a clinical decision support tool for disease free survival prediction based on joint analysis of biological, clinical and radiologic features. A previously prospectively collected cohort of ES-NSCLC patients will be considered as a training set. Tumour tissue and TME characteristics will be analysed using DNA and RNA sequencing; liquid biopsy will be used to assess free circulating DNA and extracellular vesicles; radiomics parameters will be retrieved from computed tomography images. All these features, together with clinico-pathological factors, will be integrated in a model that will enable personalised patient treatment. The developed algorithm will be validated in a prospective cohort enrolled during the timeframe of project MIRACLE.



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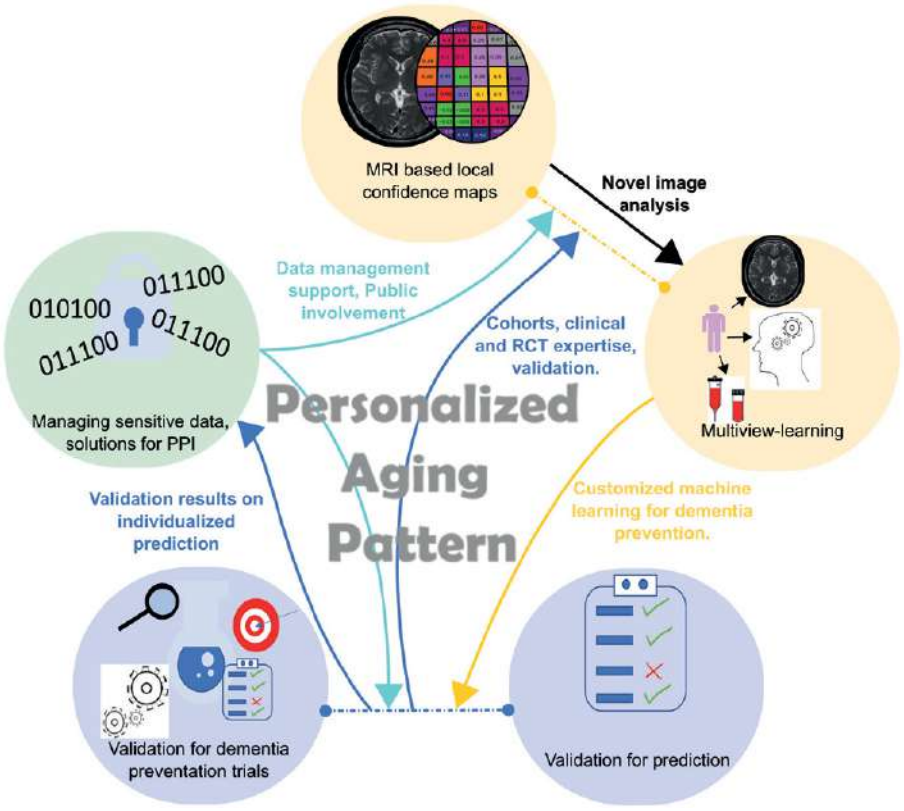
Pattern-Cog

Personalised aging pattern for early risk detection and prevention of cognitive impairment and dementia in cognitively healthy individuals

Pattern-Cog aims to improve dementia prevention strategies by developing and validating a machine learning-based personalised medicine framework for detecting the earliest signs of impending cognitive decline, enabling early and personalised multi-domain interventions. Findings from multi-domain lifestyle trials have emphasized that intervention effectiveness may be dependent on a methodology that does not yet exist, i.e., the accurate identification of at-risk individuals who are most likely to benefit. Pattern-Cog will address this methodological gap by (1) developing methods for predicting future cognitive decline based on clinical data and distinguishing between healthy individuals at higher risk for mild cognitive impairment and dementia and those who remain healthy; and (2) testing the methodology in ongoing dementia prevention trials. Instead of a standard machine learning approach, we propose an innovative concept of personalised aging pattern rooted in data from healthy individuals.



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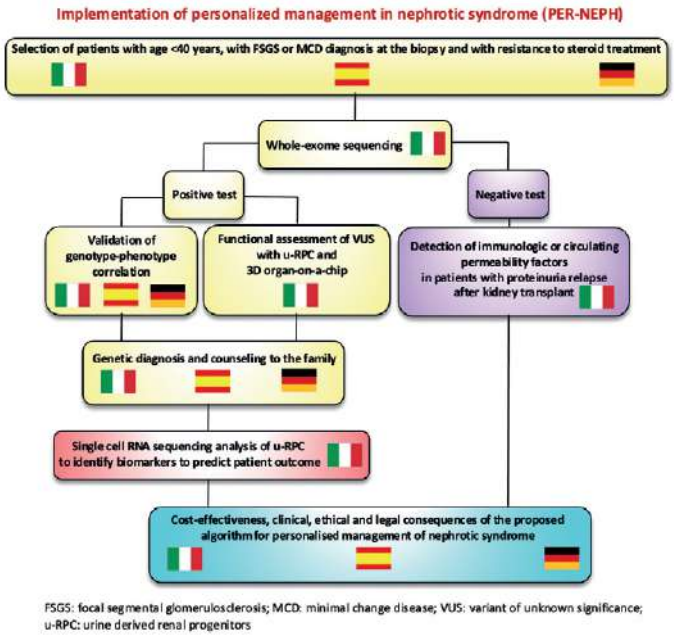
PER-NEPH

Implementation of **PER**sonalised management in **NEPH**rotic syndrome

Nephrotic syndrome in children and young adults is a medical problem of diverse pathophysiology and prognosis. Current diagnostic algorithms fail to avoid under- and overtreatment with toxic drugs as defining the underlying cause is difficult. We developed a diagnostic algorithm to stratify patients through advanced genetic testing, reverse phenotyping, and personalised disease models. This can double the current diagnostic rate in patients not responding to therapy and to predict disease relapse in those that progress to end stage kidney disease and undergo kidney transplant.

The aims of this project are:

1. Implementation of this diagnostic algorithm in selected European sites by a) selecting patients for a genetic testing, b) whole exome sequencing, c) validating genotype-phenotype correlation, and d) assessment of variants of unknown significance by functional studies with patient urine-derived renal progenitors disease models.
2. Personalising the assessment of non-genetic forms and of relapse after transplant by identifying patients negative to the genetic testing and with proteinuria relapse after kidney transplant, as well as personalising the detection of immunologic factors by super resolution microscopy and circulatory permeability factors by 3D organ-on-a-chip model system.
3. Assessing the cost-effectiveness as well as clinical, ethical, and legal consequences of this algorithm.



FSGS: focal segmental glomerulosclerosis; MCD: minimal change disease; VUS: variant of unknown significance; u-RPC: urine derived renal progenitors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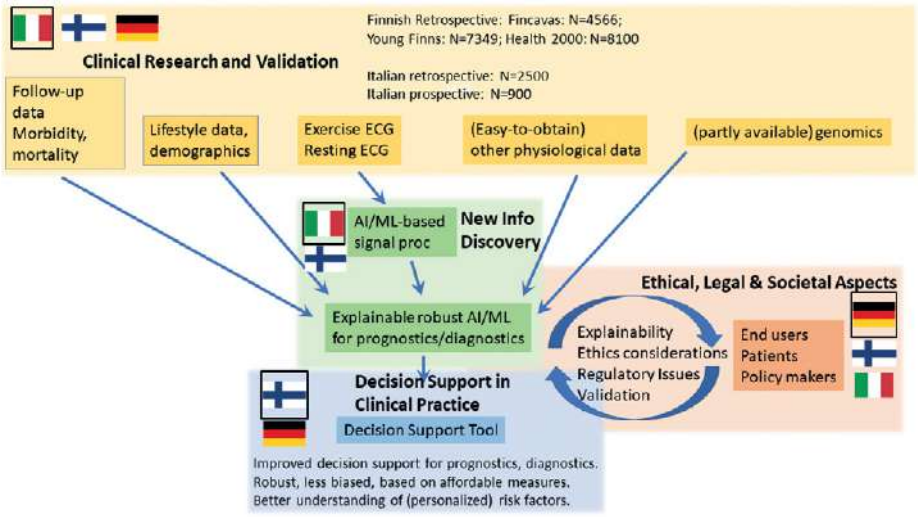
PerCard

Personalised prognostics and diagnostics for improved decision support in cardiovascular diseases

Cardiovascular Diseases (CVD) account for 45% of all deaths in Europe. Eighty percent of premature heart diseases are preventable, if personal risks can be identified early. However, currently used risk models 1) do not reflect true populations, especially with regard to gender, 2) do not give sufficient consideration to the genetic backgrounds of individuals, and 3) do not use all the information available in different data sources.
PerCard combines different data with novel analysis methods (AI, machine learning, signal processing) to deliver an improved risk modelling tool. The developed methods are explainable, practical, accessible, and affordable. Development combines existing Finnish and Italian data and new-to-be-collected data in Italy. Ethical and societal aspects, including gender and accessibility to all, receive special attention.
PerCard's international consortium is formed by Tampere University (Finland, coordinator), Polytechnic University of Milan (Italy), Centro Cardiologico Monzino (Italy), and Protestant University of Applied Sciences Ludwigsburg (Germany).



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PerFluid

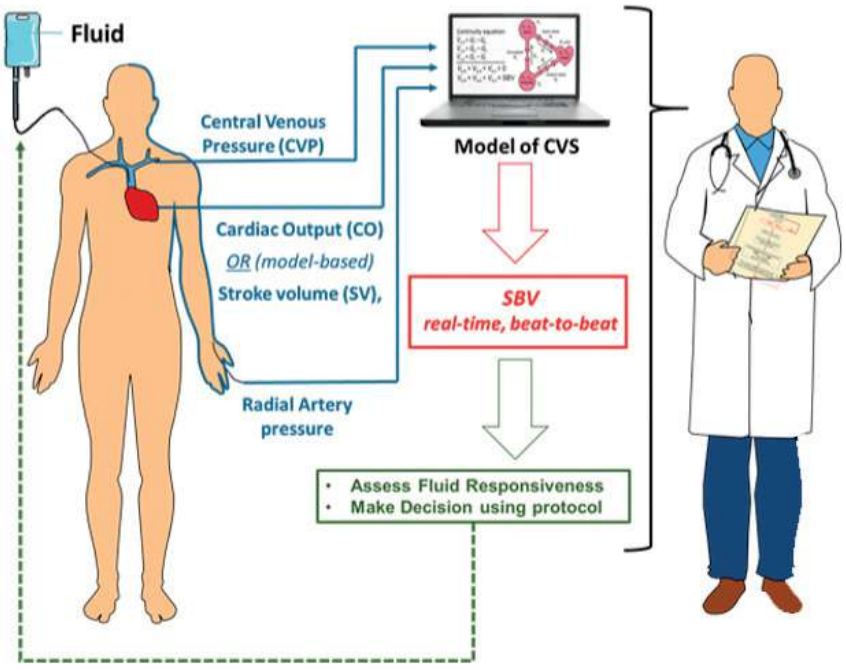
Personalised perfusion guided fluid therapy

Acute circulatory failure (ACF) and shock affect ~30% of intensive care unit (ICU) patients and occurs when the heart and circulation cannot perfuse critical organs to support their function. Adding fluid is the primary treatment to restore perfusion. However, only 50% of fluid interventions are effective. The rest have deleterious or no effect.

There is a critical need to develop a clinically feasible, low-cost means to determine which patients will respond to fluid, and which will not.

PerFluid will develop a novel model-based method to continuously measure stressed-blood volume to assess perfusion, and thus personalise fluid therapy treatment of ACF patients in the ICU. We will combine physiological models and currently available measurements to capture currently unmeasurable key physiological parameters in real-time – in particular stressed blood volume and perfusion. This metric will be combined with a novel, yet simple clinical protocol for validation in clinical proof-of-concept tests.

Using only currently available measurements makes PerFluid far more clinically feasible. The protocol is designed to integrate seamlessly with typical care practice, so no work is added. Digitally driven, it is potentially very low cost, with significant potential to address the high mortality and cost of ACF by personalising and optimising care.

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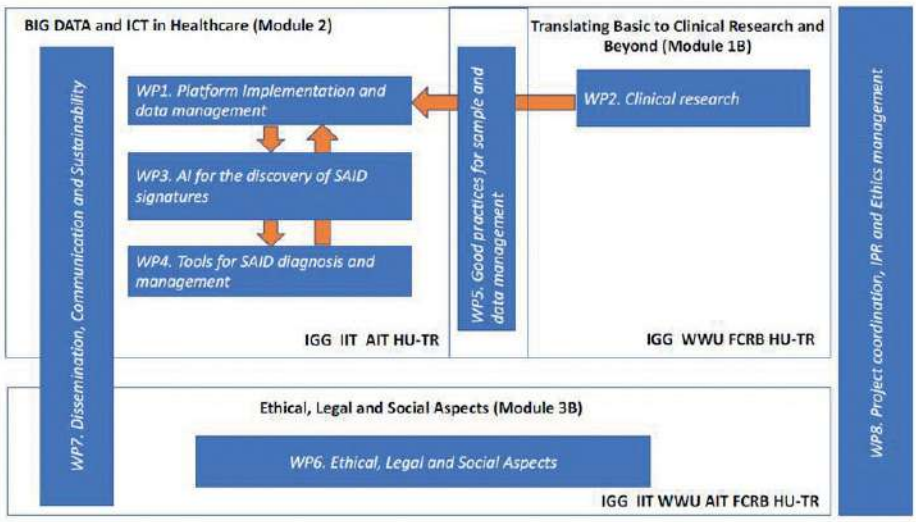
PerSAIDs
PERsonalised medicine for SAIDs

Systemic Auto-Inflammatory Diseases (SAIDs) are a growing number of rare conditions with monogenic or multifactorial genetic etiology, causing deregulation of the mechanisms that control innate immune responses. For specific monogenic SAID, personalised medicine (PM) is already an established reality. However, there is evidence that personalised approaches could be beneficial also for other SAIDs, 70-80%, known as "undefined" (uSAIDs) due to the fact that molecular testing cannot provide diagnostic confirmations.
The present proposal will link some of the largest registries and bio-sample repositories on SAIDs in Europe to i) analyse available data and produce new omics, ii) generate standardised protocols and common bioinformatics pipelines for data management and analysis, iii) simplify reuse of data in compliance with FAIR principles and GDPR. We will also develop appropriate approaches, including machine learning tools, to decode the disease complexity, thus improving SAIDs classification, diagnosis and prognosis, and supporting the discovery of novel therapies.



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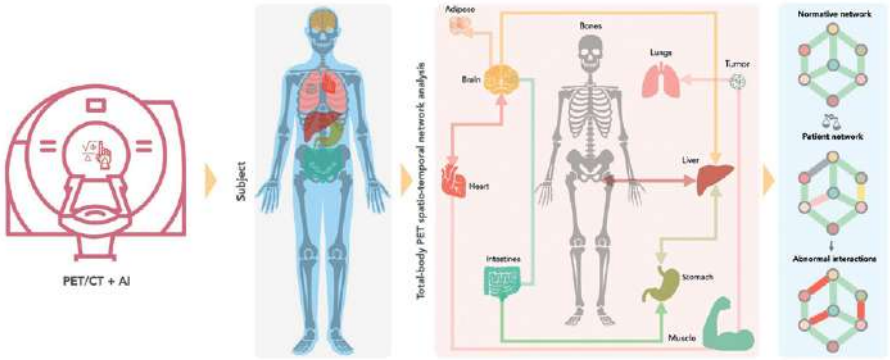
PETictCAC

Predicting risk of cachexia in cancer patients

Unintentional weight loss is common in patients suffering from advanced cancer. This condition has long been recognised as a frequent and life-threatening complication of many malignancies, but research has only recently begun to uncover its molecular basis. Clinicians refer to cancer associated cachexia (CAC) once weight loss exceeds 5% over 6 months. Therapeutic strategies to revert weight loss after it commenced are ineffective, possibly because they are initiated too late or tackle the wrong pathway. The project explores novel approaches to diagnose CAC before weight loss occurs to implement therapeutic interventions earlier.

We propose to develop a computational framework that uses artificial intelligence (AI) to support an automated analysis of interactions between organs that we can visualise and quantify non-invasively using positron emission tomography (PET). PET imaging of glucose uptake reveals the metabolic connectivity between organs and can conceivably detect the mobilisation of resources in fat and muscle tissue before weight loss weakens the patient. If successful, our computational framework will be developed into a clinical decision-making tool integrating ethical and legal considerations. This tool will determine individual patient risk to develop cachexia and, thus, support personalised therapeutic interventions.

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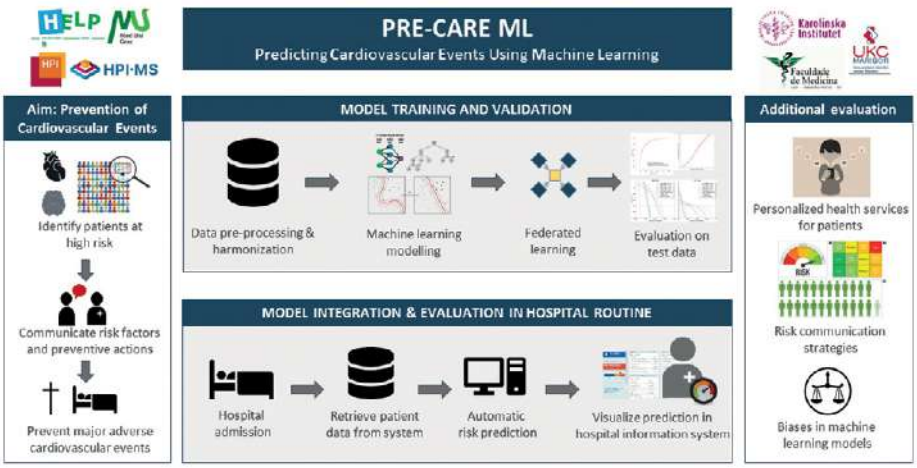
PRE-CARE ML

Predicting cardiovascular events using machine learning

Cardiovascular disease is the leading cause of death and causes tremendous suffering, socioeconomic loss, and burden to health systems. Atherosclerosis, a condition that is clinically silent, i.e. it often remains undetected until it is too late, underlies major cardiovascular events such as heart attacks and strokes.
Early identification of people at high risk for such clinical events enables preventive actions. However, conventional risk prediction scores are often not widely adopted in otherwise healthy and symptom-free people. At the same time, medical information is increasingly digitalised. This leads to huge amounts of electronic health data amenable to risk prediction. Yet, conventional approaches fail to handle these data in its entirety and harness it for medical decision-making.
Here, we use artificial intelligence (AI) methods to develop modern risk prediction tools for early identification of people at high risk for major cardiovascular events. This endeavor builds on our previous experience in using machine-learning algorithms for risk prediction. In our multidisciplinary consortium, we aim to validate and improve our models across different hospital networks and populations. Second, we will integrate our models in hospital information systems and assess their impact on daily hospital routine. Lastly, we will address effective risk communication strategies in order to effect behavioral changes in patients.
Our ultimate aim is to develop easy-to-use, accessible, and reliable risk prediction tools that allow early identification of people at high risk in order to set actions to prevent major cardiovascular events and thereby reduce the global impact of cardiovascular disease.



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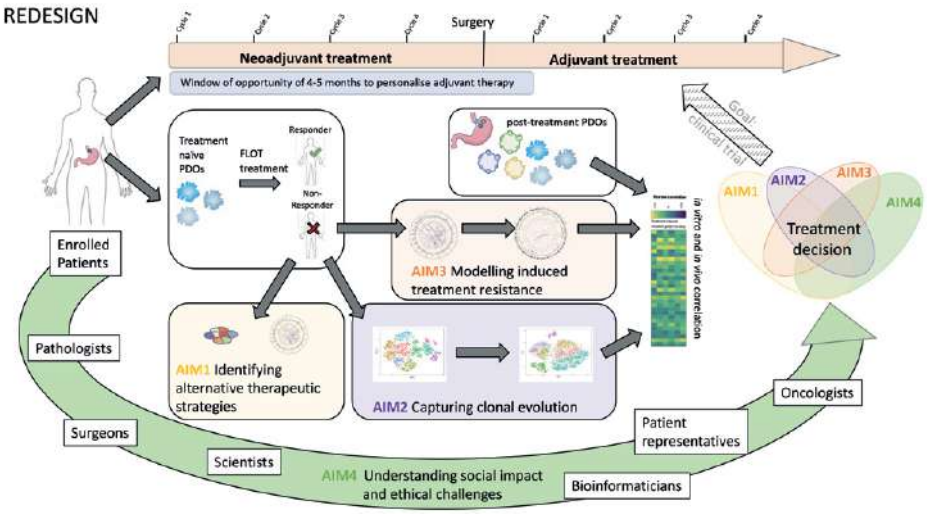
REDESIGN

Treatment decision based on organoids in gastric cancer

The REDESIGN consortium proposes a multidisciplinary programme based on patient-derived organoids (PDOs) to guide personalised treatment in gastric cancer (GC) patients. Standard-of-care for locally advanced GC in Europe is neoadjuvant FLOT chemotherapy. Pathological response to neoadjuvant treatment is directly linked to overall survival. However, 63% of patients show resistance to the treatment and have no pathologic major response after treatment. Two different mechanisms are important in the aetiology of resistance: intra-tumoural heterogeneity and the accumulation of mutations that circumvent the point of action of a given drug. Deciphering intra-tumoural heterogeneity and predicting mutations that emerge under selective pressure of treatment will enable early identification of upcoming drug resistance, allowing tailored treatment strategies before the start of treatment.
We propose to integrate functional drug response data from PDOs from pre-and post-treatment specimens, dissecting clonal evolution and mutational adaptation of PDOs under selective treatment pressure, as well as CRISPR/Cas9 engineered human organoids. The consortium aims to unravel treatment resistance mechanisms and design treatment strategies that consider the identified causes of resistance. Further, the patient's point of view will be taken into account in personalised treatment decisions. The overarching aim is to improve personalised treatment by combining the gained knowledge of evolutionary trajectories and mechanisms of resistance to therapy as well as addressing ethical and social challenges when using PDOs to aid clinical decision making in the era of precision medicine.



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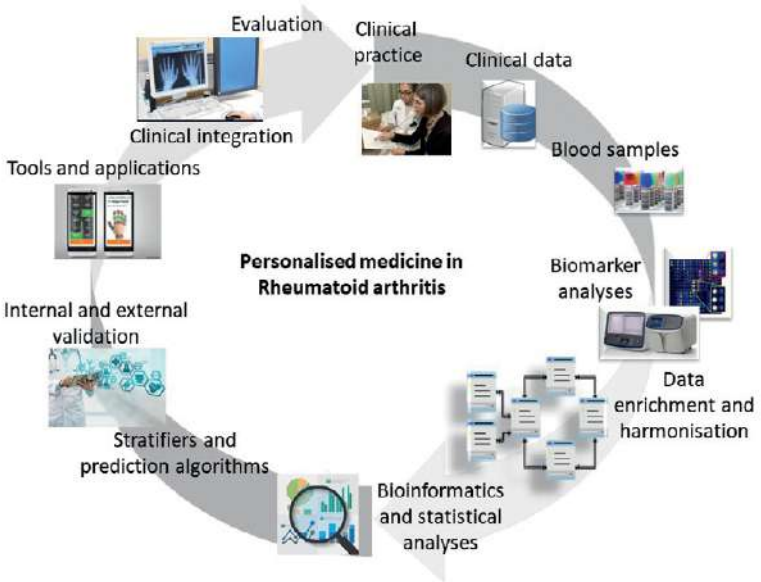
ScandRA

Personalised medicine in RA by combining genomics, biomarkers, clinical and patient-data from the Scandinavian countries, and by integrating the knowledge generated into routine care

Rheumatoid Arthritis (RA) is a chronic disease that displays a significant variation in clinical picture, response to therapy, and longer-term outcomes. With few and crude predictors available, our means for an individualised strategy are limited. A personalised medicine (PM) approach to RA requires new biomarkers, and algorithms, to support diagnosis and choice of effective treatment. For PM to transform clinical rheumatology practice, new tools to bring such algorithms to patients and to clinical practice are needed. ScandRA builds on our successful collaboration between academia, healthcare, patients, and the private sector in biomarker technologies, data interoperability and e-health. In the Scandinavian countries, we have collected large amounts of information on patients with RA in our longitudinal prospective registers and biobanks, the largest and most detailed world-wide. We are now uniquely positioned i) to make detailed clinical data on RA disease activity, treatment, and life-style available for joint analyses with novel genomic- and biomarker-data from blood samples from these cohorts, ii) to take the next step, towards integration of the emergent results into clinical practice. Planned work include i) knowledge generation from novel analyses of our RA data, ii) value creation through development of decision support tools based on these insights, and iii) work with the ethical, legal and social challenges that are necessary for successful implementation.



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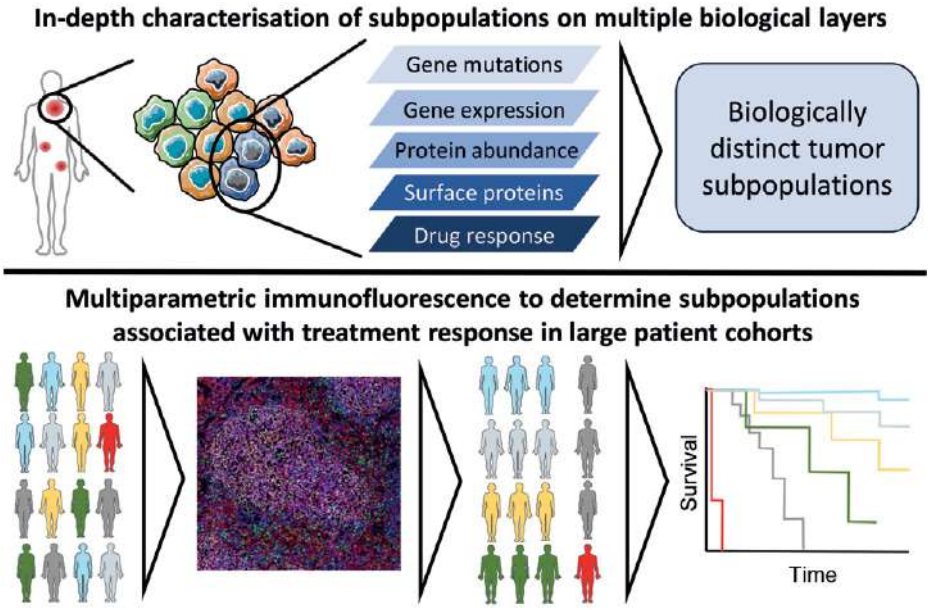
SYMMETRY

Subpopulation heterogeneit**Y** and **M**icroenviron**M**ental **E**ngagement as predictors for **T**reatment **R**esistance in l**Y**mphoma

Lymphomas, like most other cancers, consist of multiple distinct cancer cell populations within each patient. These tumour subpopulations have distinct genetic and biological characteristics leading to different drug response profiles. We will characterise these tumour subpopulations in aggressive lymphoma on multiple biological levels including gene mutations, gene expression, protein abundance, surface protein profiles, and drug response. Using the in-depth characterisation of subpopulations in the discovery cohort we will investigate large clinical patient cohorts with multiparametric immunofluorescence and describe the association of subclonal histology and response to chemotherapy. The improved understanding of tumour subpopulations and their impact on therapy efficacy combined with the ability to detect those subpopulations in diagnostic biopsies using multiparametric immunofluorescence has the potential to improve treatment stratification and thereby patient survival while reducing side-effects and treatment costs. We will perform in-depth interviews with patients treated in our centers for personalised medicine to optimise the communication of increasingly complex diagnostic and therapeutic procedures in personalised medicine. These data will be complemented by quantitative surveys to create communication guidelines for personalised medicine.



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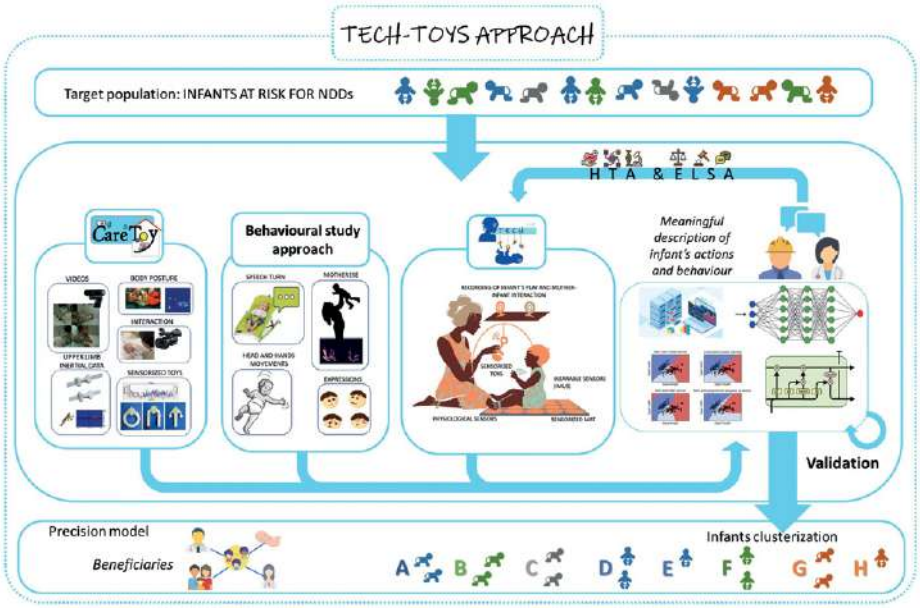
TECH-TOYS

Acquire digi**T**al biomark**E**rs in infan**C**y wit**H** sensorized **TOYS** for early detection and monitoring of neurodevelopmental disorders

Neurodevelopmental disorders are a group of frequent (1/10 children) sensori-motor, cognitive, communication, learning, behavioural disorders of multifactorial aetiology, with onset early in life but with life-long consequences. Despite advances in our understanding of aetiology, diagnosis and start of intervention are often late (many months after onset of first clinical signs) and not based on quantitative data. TECH-TOYS aims to develop a new technological home interactive play setting (i.e. a gym equipped with a sensorised mat, a set of sensorised toys, wearable inertial movement units and cameras) to provide easy-to-handle quantitative digital biomarkers of infant's neurodevelopment and infant-caregiver interaction. Previously acquired big data and new data collected prospectively on motor behaviours, together with gaze activities and social competence in infant-caregiver interaction, will provide an Explainable Artificial Intelligent Precision Model for early detection of atypical features. Ethical, Legal, Social aspects (ELSA) and Health Technology Assessment (HTA) will provide key factors in decision-making process and cost effectiveness analysis. Moreover, parents' organisations will have a strong involvement in the project activities and in the Ethics Monitoring Board and will contribute to the design of platform and of the Personalised Precision Model. The results will open new frontiers for early, timely, personalised, home based, quantitative detection of neurodevelopment in the first months of life.



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WODIA

Personalised Medicine Screening and Monitoring Programme for Pregnant Women Suffering from Preeclampsia and Gestational Hypertension

Half a million women die each year giving birth. The two pregnancy-related blood pressure complications, **preeclampsia and gestational hypertension, are the cause of 76,000 mothers & ½ million infants dying each yea**r. Infants who survive often **experience long-term health problems**, including cerebral palsy, chronic lung disease, blindness & hearing loss, and the resulting societal healthcare costs are high.

Existing work has proposed a range of screening procedures and algorithms for detecting those pregnancies that will later develop preeclampsia or gestational hypertension. However, these are resources intensive for the service providers to implement, and challenged with a high false positive rate of up to 10%.

With the **WODIA project we aim to make it safer for women to give birth by identifying and tracking the early signs of preeclampsia and gestational hypertension while the complications are still preventable, by developing a personalised medicine screening, therapy, and home monitoring service.**

WODIA will **combine the maternal characteristics with a range of biomarkers. Together, these will allow for more effective targeted personalised medicine with individual medication dosing and fewer and more effective clinical visits.**