✚ ERA PerMed

NEWSLETTER 9
January 2023

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 2022

PREVENTION IN PERSONALISED MEDICINE
24 successful consortia are funded with a total investment of approximately 30.2 million Euros for three years

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NEWSLETTER 9

Looking back at 2022 and into the future

A new exciting year has begun, and with it we enter the final year of ERA PerMed. In the past year, 2022, ERA PerMed has carried out and participated in various activities. During the summer we have launched a video competition "the story behind our personalised medicine research project" for the young researchers participating in the JTC2018 co-funded projects. We have received 9 videos from different consortia and the best video was determined by votes from the public and ERA PerMed partners. Just recently we announced the results of the competition with the top three places being very close. Ultimately, the video of project RADprecise won the competition, project PersTIgAN received 2nd place and project JAKSTAT-TARGET arrived at 3rd place. All the videos can be viewed on the ERA PerMed website or ICPerMed YouTube channel.

In October, an online midterm seminar was held for the JTC2019 projects, in which the coordinators of the 22 funded projects presented the advancement and current outcomes from their projects. It was encouraging to see that despite the major impact of the Covid19 pandemic, many of the projects have managed to make significant progress.

Throughout the past year and to date, ERA PerMed representatives are busy working together enthusiastically with ICPerMed and other stakeholders, on developing the European Partnership for Personalised Medicine (EP PerMed). Regular updates on the activities around the development of EP PerMed can be found on the ERA PerMed website.

As we enter the final year of ERA PerMed, we are looking forward to continue following up on the outstanding progress our funded projects are making. We are fortunate that at the end of February we will be able to carry out a grand face-to-face final symposium in which we will hear all about the outcomes of our 25 JTC2018 projects, which were co-funded by the European Commission. The symposium will also include a panel discussion with patient representatives on the topic of patient involvement in personalised medicine research from which we hope to learn lessons on how to better involve patients in the future EP PerMed. To express ERA PerMed's support for young researchers, a young researcher from the RADprecise consortium, representing the winning video, has also been invited to the final symposium to showcase the video and give a short talk about the research being done and the effect that participation in such a collaborative project had on their scientific career.

Finally, this past year we have executed our 5th non-co-funded call for proposals, JTC2022, on 'Prevention in Personalised Medicine' of which you can read about in more details in this newsletter. While there are no more calls for proposals from ERA PerMed, new funding opportunities in the field of personalised medicine are expected to come from EP PerMed starting in 2024.

With this, we wish you all excellent and pioneering research, productive collaborations and meaningful advancement in promoting personalised medicine worldwide this New Year 2023!

Joint Transnational Call for Proposals 2022:
PREVENTION IN PERSONALISED MEDICINE

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, 33 funding organisations of 26 countries, 7 regions and one charity agreed to launch the fifth and final ERA PerMed Joint Transnational Call (JTC) for collaborative innovative research projects in PM. A general prolongation of the ERA-Net funding programme ERA PerMed allowed the implementation of this unforeseen fourth additional call that is not receiving co-funding through the European Commission but is exclusively supported by the regional and (inter)national funding organisations and the charity.

With the Joint Transnational Call for Proposals 2022, ERA PerMed fosters research and innovation activities in prevention in PM. The overarching goal of the call is the development of tailor-made strategies for prevention of disease and disease progression, at three different levels:

i.   Preventive measures decreasing the rate of incidence (primary prevention)
ii. Early detection to increase the efficacy of a preventive therapy, even before symptoms are developed (secondary prevention)
iii. Interventions preventing disease recurrence or improving patients' care and quality of life (tertiary prevention).

Four additional funding organisations, which are not part of the ERA PerMed Consortium, joined through this JTC2022 the ERA PerMed calls for the very first time: The Research Council of Lithuania, (LMT), Lithuania, the South African Medical Research Council, (SAMRC), South Africa, Sweden´s Innovation Agency, (VINNOVA), Sweden and the Ministry of Science and Technology, (MOST), Taiwan. Therewith, ERA PerMed, as the biggest ERA-Net in the health sector, has engaged, in total, 42 funding organisations participating in five joint transnational calls, including regional and international funders of 32 countries and five continents.

In the JTC2022, 171 eligible pre-proposals were submitted, 60 consortia were invited to submit a full-proposal and 24 proposals with a total funding volume of 30.2 million Euros will be funded!

1st EU-Africa PerMed Summer School Standards in Personalised Medicine Research

22-23 February 2023
Cape Town, South Africa

Around 40 applications from both African and European countries have been received. Selected candidates will be informed during the last week of January

HAVE A LOOK AT OUR PREVIOUSLY FUNDED PROJECTS
here

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BIPCOM
Medical comorbidities in bipolar disorder: clinical validation of risk factors and biomarkers to improve prevention and treatment

Bipolar Disorder (BD) is a common, heritable, chronic, and recurrent disorder that represents a critical public health problem, due to its prevalence, its high degree of disability and psychiatric and medical comorbidities (MC). The project on "Medical comorbities in bipolar disorder: clinical validation of risk factors and biomarkers to improve prevention and treatment" (BIPCOM) aims to study MC in people with BD targeting 2 main objectives: (1) to identify prevalence rates, risk and protective factors and natural history of MC among subjects with BD, through analyses of the Nordic medical registers and a cross-sectional study exploiting existing datasets of patients with BD; (2) to conduct a clinical study involving 400 subjects to assess the overall clinical profile of these patients and study the onset of medical comorbidities. BIPCOM will be implemented through continuous consultations with stakeholders (scientific and patients' associations, users, and families), for ensuring results' acceptability and transferability.
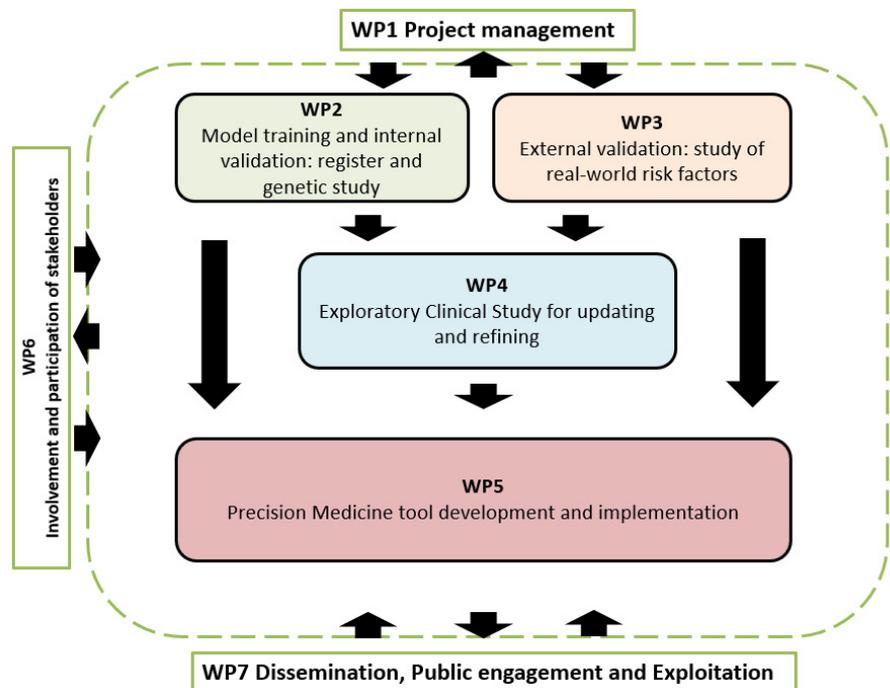
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DAWN-AF
Digital Twins to Treat Atrial Fibrillation

Atrial Fibrillation (AF) is the most common cardiac arrhythmia. Since AF is progressive, the longer one has it, the harder it is to treat, and the risks of stroke, dementia and heart failure increase. The most effective treatment is catheter ablation therapy, a procedure that strategically destroys tissue to restrict propagation of electrical waves. However, approaches are currently generic, ignoring patient variability in atrial structure, and AF usually recurs. We aim to develop a personalised medicine approach based on computer modelling, to use digital twins to plan AF ablation to prevent recurrence. We propose to use preoperative measurements, imaging (MRI/CT) and the ECG, to build digital twins. However, these data are insufficient to uniquely characterize the atria, so we will build sets of potential digital twins for each patient, each of which will have its ideal ablation treatment determined. Invasive measurements acquired during the ablation procedure will be then used to select the digital twin that best matches the patient. Economic analysis will evaluate benefits arising from early preventative and longer-lasting treatment, reduced duration and procedural risks of interventions.
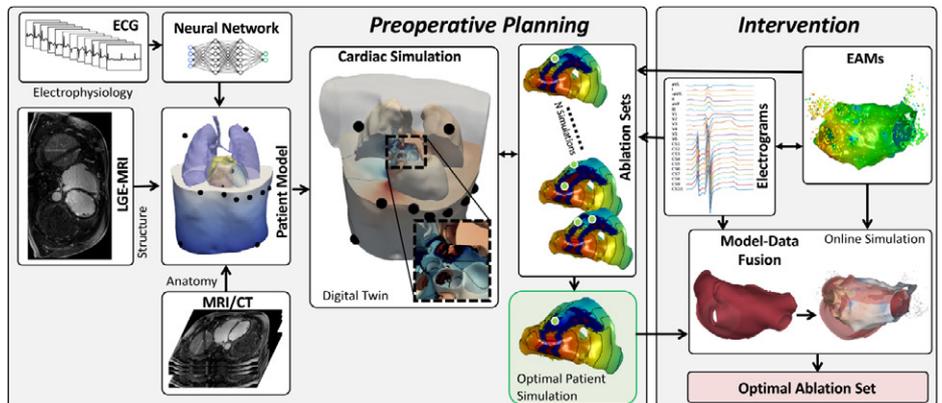
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DEEPEN-iRBD
Prodromal DEtErminants for PhENoconversion of idiopathic RBD to alpha-synucleinopathies (PD, DLB and MSA)

Evidence shows that individuals affected by idiopathic REM sleep behavior disorder (iRBD) have a high risk of conversion to Parkinson's disease, or dementia with Lewy bodies, or multiple system atrophy. Despite sharing a cellular pathological hallmark, the aggregation of alpha-synuclein, and some clinical features in the early stages, these conditions show different phenotypes in later stages with significant therapeutic and prognostic consequences for the patients. The consortium DEEPEN-iRBD aims to develop a pathogenicity model for prediction of phenoconversion utilizing pre-clinical/clinical research and data analysis, taking into account a personalised medicine approach, based on the individual's unique characteristics and optimisation of strategies for the prevention, diagnosis and treatment of the individuals rather than the disease. In this project, both existing and newly acquired data will be integrated, including advanced clinical assessments, physiological signal recordings, molecular markers derived from body fluids, skin biopsy, and iPSC-derived brain cells, in order to identify a specific profile at a very early stage, that is a prodromal phase, for each of the above conditions. This would ultimately allow to define a model for early risk stratification, diagnosis, treatment, and prognosis of patients with iRBD. A further important objective of the project deals with the ethical and social aspects of screening people in a prodromal stage of the diseases and of communicating the screening results.
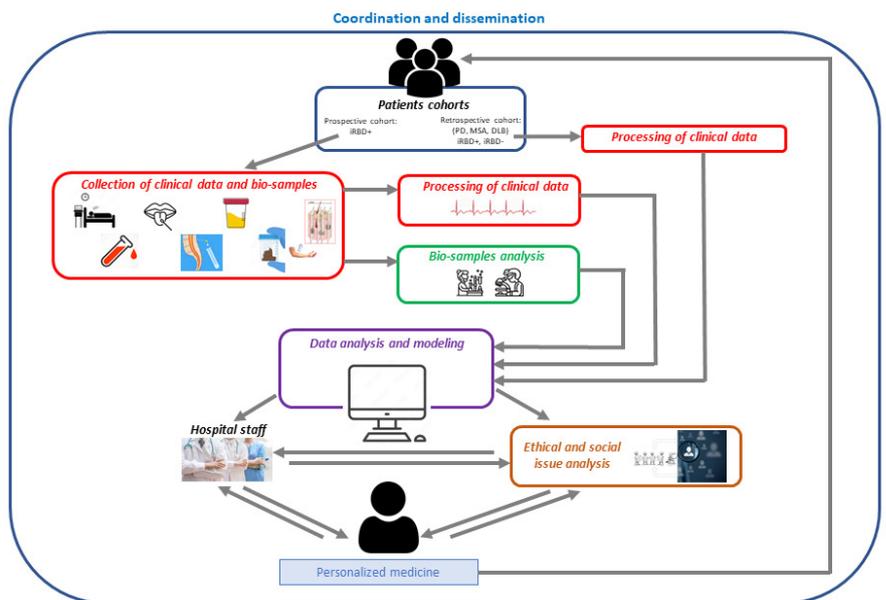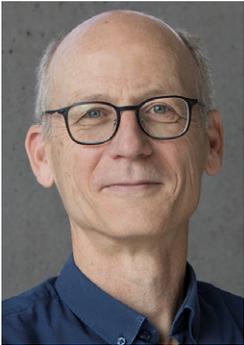
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ETAP
Early diagnosis and personalised Therapy in Autism spectrum to Prevent severe disorders

Problem: Autism Spectrum Disorder (ASD) is growing (1-in-44 children; 4:1 boys:girls) and manifests in debilitating cognitive problems. "Social blindness", the inability to recognise emotions in others, is a common debilitating feature, treated via intensive 1:1/ small-group therapy. It is costly, in very short supply, and thus often infrequent. Growing ASD diagnosis, particularly in boys, threatens to create a "lost-generation" unable to achieve their full potential.
Need: To prevent severe disorder by significantly increased access to emotional recognition training/therapy for those with ASD, and at low(er) cost.
**Proposed Solution:** To virtualize emotional recognition training in a two-way adaptive, and individualized system by combining three *novel* key elements (**KE1-3**)
KE1: Realistic avatars able to show detailed emotions (*Availability, Scalability, Reproducibility*)
KE2: Sophisticated sensing to read subject emotional state, reaction rates in therapy tasks, stress levels, to create critical subject feedback (*Personalisation*)
KE3: Programmed therapeutic methods to challenge and respond to measured subject response (*Adaptive, Gamified*)
Outcome: Highly extensile software-based platform technology solution to dramatically increasing access and scalability, lower costs, and create new insights/pathways in ASD research.

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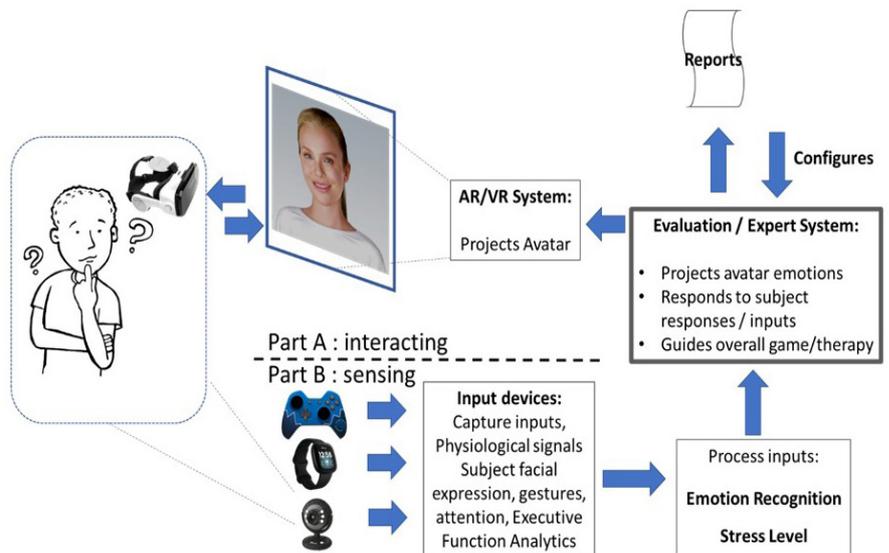
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Glioma-PerMed
Glioma invasion assays as a predictive tool for personalised glioma medicine

Glioblastoma multiforme (GBM) is the most frequent malignant brain tumor, which consists of highly invasive glioma stem cells (GSCs). No cure exists, and GBM patients' median survival is <24 months. Therefore, a therapeutic strategy to perturb GSCs invasion in the human brain is critical. Since GBMs are highly heterogeneous and are unique from patient to patient, "one therapy for all" is not practical. Furthermore, invasive behavior is unpredictable in the human brain. The "Glioma-PerMed" is establishing an interdisciplinary research consortium aiming to develop personalised glioma invasion assays in the preclinical models of human brain organoids and zebrafish brains. We will quantitatively determine the GBM invasion behaviors with unbiased machine learning algorithms. As our "personalised glioma invasion assay" platform allows drug screenings, we will screen an FDA-approved drug library and identify molecules that can be transferred to clinical patients. Ultimately, these would be the first step towards personalised GBM medicine.
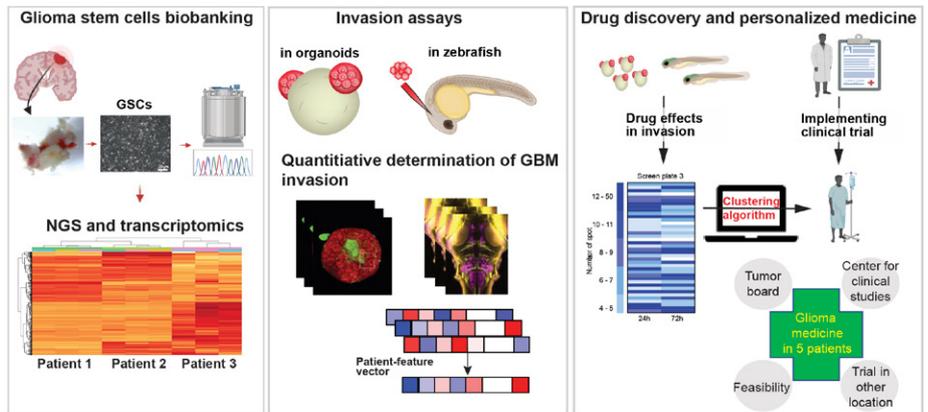
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IPerGlio
Improving personalised glioblastoma care by intertwined immunomics and artificial intelligence approaches

New treatment strategies to improve glioblastoma patient care and quality of life are urgently needed. Survival rates are very poor as virtually all glioblastomas recur and standard therapy has not changed for over 15 years. Around 25% of clinical trials in glioblastoma evaluate immunotherapies and several have reported long-term survival benefits in 10-20% of patients. We currently lack biomarkers to predict clinical benefit of immunotherapy in this highly heterogeneous disease.

The objective in IPerGlio is to consider clinical and immunological data integrated with sex and age as well as key lifestyle and environmental factors using artificial intelligence (AI) technologies. This represents a novel approach to guide personalised interventions improving glioblastoma patient care and quality of life. By applying AI generated models to these data, IPerGlio will deliver prognostic markers that can be used to guide decisions for combination treatment with immunotherapy in clinical trials. Furthermore, IPerGlio will address the ethical challenges concerning data security and sharing posed by personalised medicine and AI approaches through active stakeholder and patient involvement.

The IPerGlio project will strongly improve clinical decision-making for glioblastoma patients by identifying risk factors amenable to reinforce tertiary prevention and ensuring effective and responsible delivery of AI-guided personalised immunotherapy.
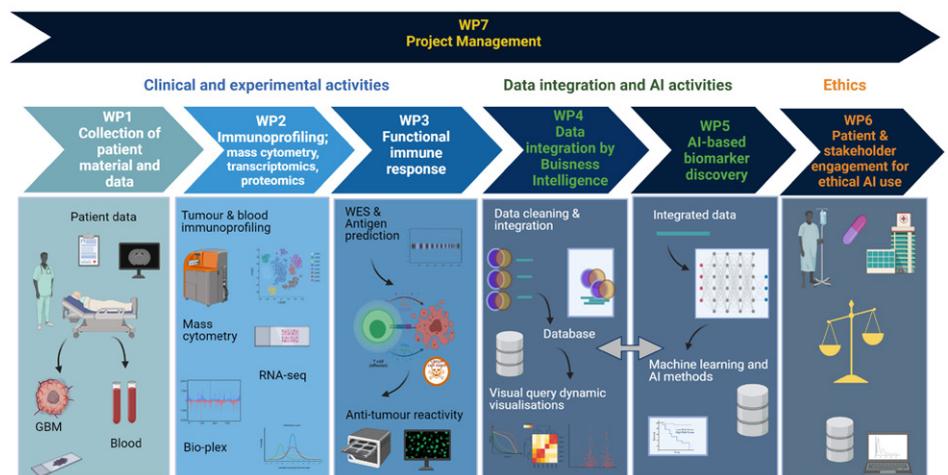
Project figure created with BioRender.com

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KidneySign
An integrated multi-omics signature of kidney fibrosis for CKD precision medicine

Chronic kidney disease (CKD) is a progressive condition defined by sustained structural or functional abnormalities. Monitoring and predicting the risk of CKD progression is difficult due to fluctuating renal function markers and limited access to the organ itself for structural assessment. The KidneySign project aims to develop a blood- and urine-based multimodal proteomic signature reflecting in situ kidney fibrosis and predictive of CKD progression. Personalised nephroprotection based on the complementarity of patients and drugs proteomic profiles will also be explored. The resulting clinical decision support system providing risk estimates and therapeutic guidance will comply with ethical and societal issues identified at each stage of the project. The project relies on the analysis of Big Data comprising classical, proteomic and peptidomic evaluations of kidney biopsy, urine, serum and plasma samples from existing patient cohorts, biobanks and a KidneySign prospective study.
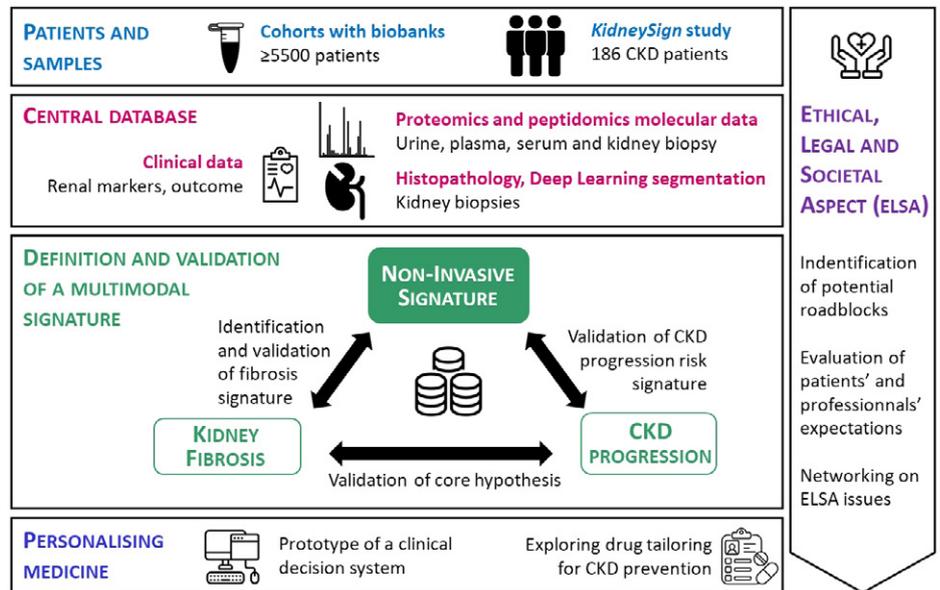
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LANTERN
Lung cancer multi-omics avatars for integrated precision medicine

Current management of lung cancer patients have reached a high level of complexity, thereby complicating the process of decision-making by clinicians. With the advent of advanced Artificial Intelligence (AI) techniques, various omics datasets may be used efficaciously in creating predictive models.

LANTERN partners will develop accurate predictive models for lung cancer patients, through the creation of Digital Human Avatars (DHA), defined as computerised representations of individual patients with a focus on biological functions.

LANTERN partners will prospectively enrol 600 lung cancer patients, collecting several omics domains (including radiomics and genomics). Advanced and correlated omics variables will be modelled, originated and parameterized in an experimental context of cutting-edge big data. The development of DHA and the consequent application of AI-based predictive models in clinical practice will in fact, favour the accuracy of diagnosis and a complete personalisation of treatment.
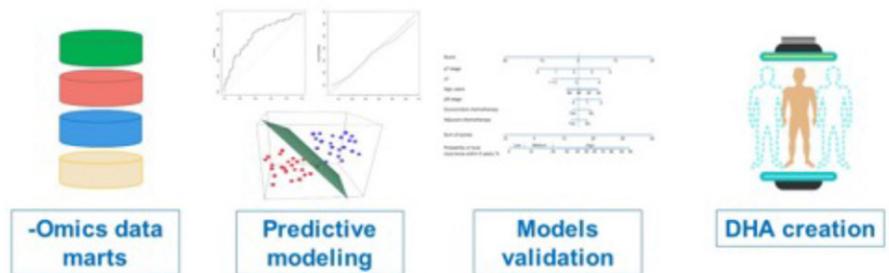

Figure: A brief description of the different steps involved in the LANTERN project. The LANTERN project will manage multi-omics data obtained from 600 lung cancer patients and with an advanced AI-based analysis will develop (and validate) accurate predictive models. The creation of a Digital Human Avatars (DHA) will pave the way for complete personalised treatments.

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MG-PerMed

Personalising myasthenia gravis medicine: from "one-fits-all" to patient-specific immunosuppression

Myasthenia Gravis (MG) is a prototypic autoimmune disease causing muscle weakness and fatigability, frequently treated with lifelong immunosuppressive therapy (IST). Clinical heterogeneity, unpredictable disease course, treatment refractoriness in a proportion (10-15%) of patients, IST-related adverse events, and inter-individual variation in response to both conventional IS and emerging biological drugs highlight the need to adopt more effective, preventive and safe personalised medicine (PM) strategies, still lacking in MG. The MG-PerMed project will combine pre-clinical, clinical, artificial intelligence (AI), telemedicine and bioethics research to promote adoption of PM in MG clinical practice. Integration of biomarker with real-world clinical data from three MG populations (Italian, French and Israeli) via AI will allow the development of a clinical decision support tool (MG-CDST), whose effectiveness in guiding the choice of the best patient-centred treatment programme will be proven in an exploratory clinical study. Our findings will set the basis for a shift from the current "one-fits-all" treatment flow-chart to personalised care in MG, thus promising to significantly improve therapeutic success and MG patients' quality of life.
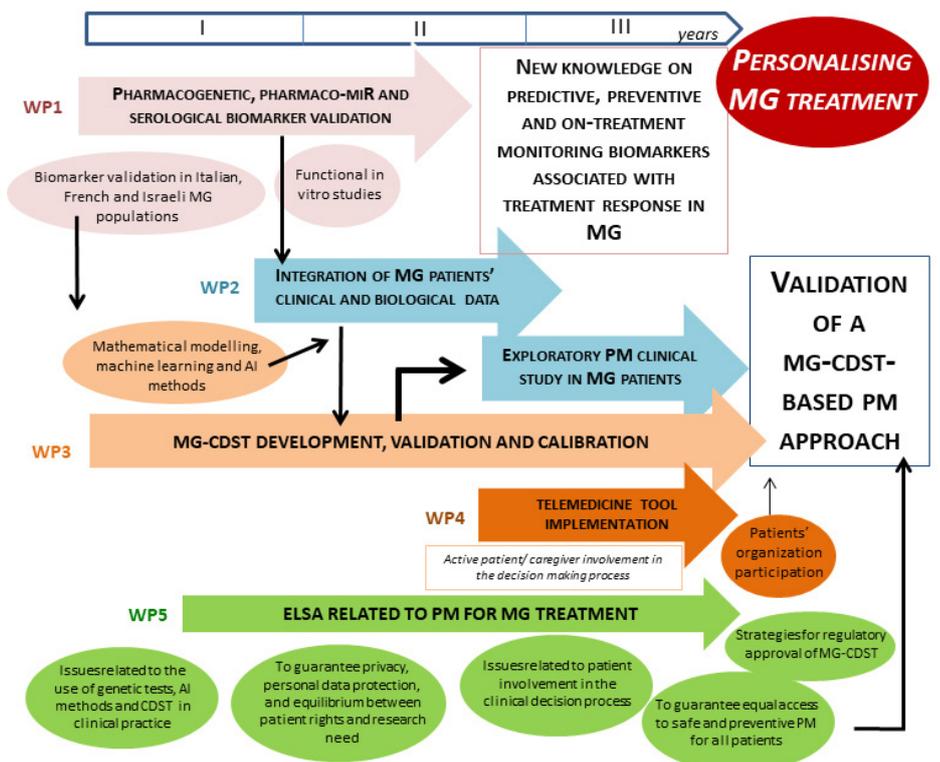
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miRPOC
miRNA as biomarkers in early detection and personalised treatment in ovarian cancer

Ovarian cancer is generally diagnosed at a late stage, after the disease has spread and has poor survival diagnosis. Currently, there are no effective early detection strategies and early disease symptoms are non-specific (e.g., bloating, feeling of fullness). Biomarkers evaluated to date, do not outperform the "best available" marker CA125; however, a preliminary study provided evidence that a serum microRNA profile may provide better differentiation between ovarian cancer cases and non-cases than CA125. This study will provide validation of a microRNA panel for early detection of ovarian cancer in serum samples from prospective cohorts and clinical data and biospecimens. The overarching objective is to validate a serologic microRNA panel that, together with CA125, would have sufficient diagnostic discrimination for early-stage disease to be used as a tool that, complementary to imaging, would allow early diagnosis and direction of patients with suspected malignancy to personalised gyn-oncological care.
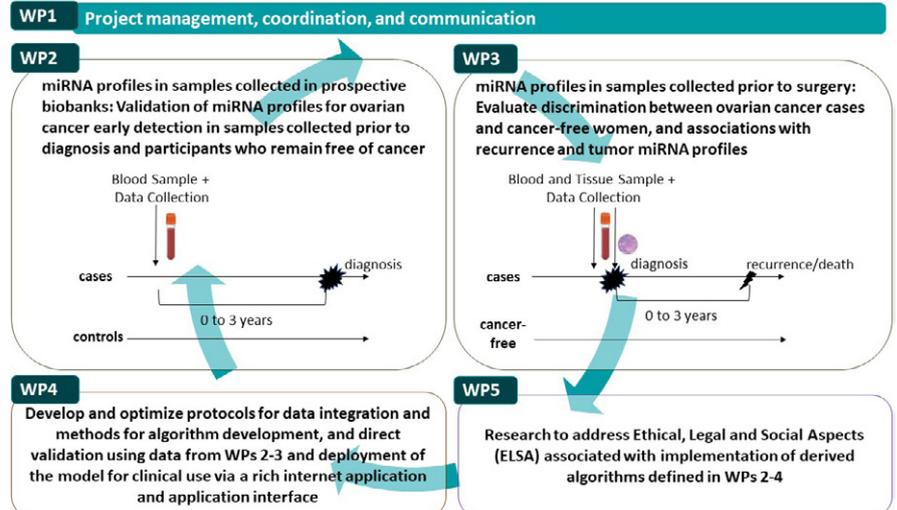
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OmegaPerMed
Optimizing omega-3 supplementation to resolve inflammation in a personalised medicine cardiovascular disease prevention

Cardiovascular diseases (CVD) are the most common cause of death in Europe and worldwide. Although omega-3 polyunsaturated fatty acids (PUFA) are traditionally considered beneficial in CVD prevention, clinical trials have generated contradictory results for CVD outcomes. The aim of this project is to generate a personalised CVD prevention decision tool to identify responders and non-responders to omega-3 treatment. This project will explore observational cohorts and clinical trials for the interactions between genes, omega-3 PUFA treatment and/or intake, CVD risk factors, and biomarkers, followed by data integration for artificial intelligence (AI)-empowered development of the OmegaPerMed decision tool. The resulting personalised omega-3 treatment indications in CVD can be the first personalised medicine to be widely implemented in international CVD treatment guidelines to the benefit of a large patient population.
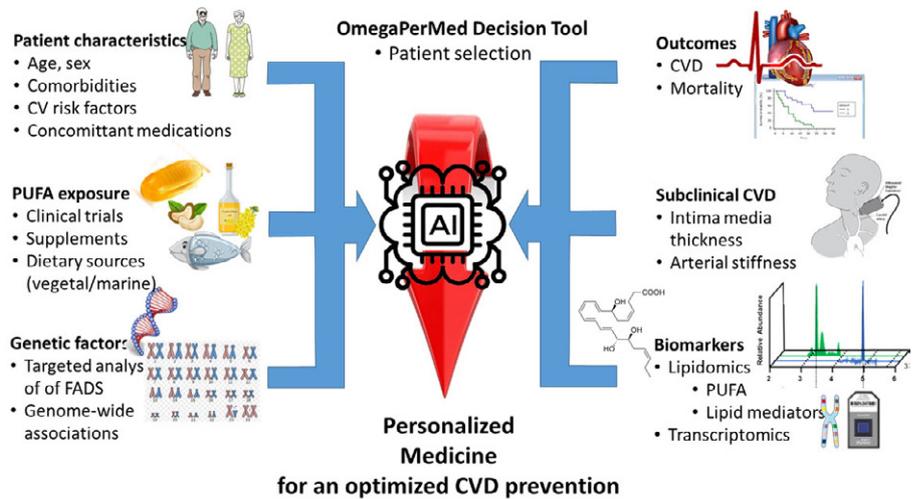
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ONAKI-ICI
Towards a personalised clinical management of oncologic patients with acute kidney injury associated to immune-checkpoint inhibitors

Treatment with immune checkpoint inhibitors (ICIs) has led to increased survival rates of cancer patients, who were previously untreatable, by favouring an immune response against tumour cells. ICIs action is not selective and may cause immune-related adverse events. Up to 29% of cancer patients, who receive ICIs treatment, develop acute kidney injury (AKI) secondary to ICIs use (ICI-AKI), and acute tubulointerstitial nephritis (ATIN) is the most frequent lesion. ICI-AKI is a serious complication that increases the risk of AKI recurrence after ICIs rechallenge and mortality. The diagnosis of ICI-AKI is performed by a kidney biopsy, which is highly invasive. We will collect retrospective and prospective demographic and clinical data of ICI-AKI patients as well as urine, blood and kidney tissue samples of ICI treated cancer patients during two years to identify novel biomarkers related to immune response to avoid kidney biopsy. This approach will allow personalising clinical management of these patients and improving their quality of life.

ONAKI-ICI: Towards a personalized clinical management of oncologic patients with acute kidney injury (AKI) associated to immune-checkpoint inhibitors (ICIs)
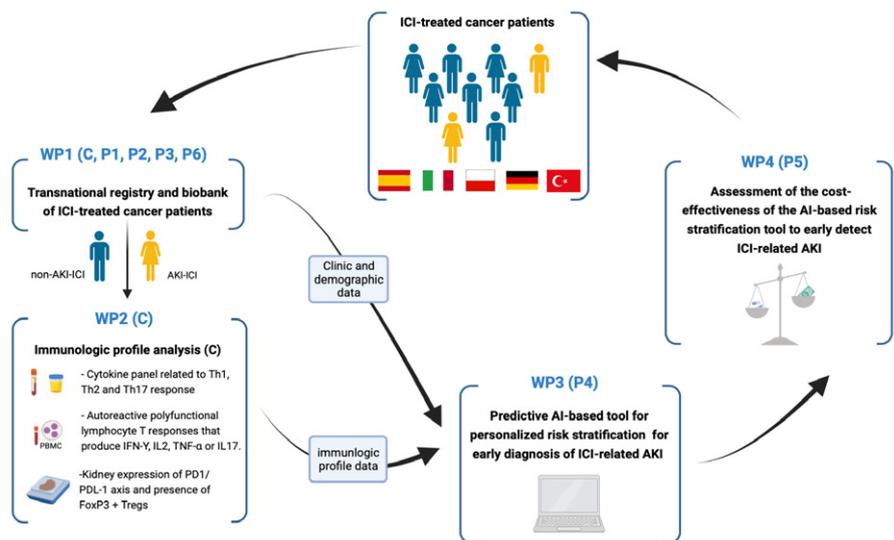
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OPTIMA
Omics Approach for Personalised Prevention of Type 2 Diabetes Mellitus for African and European Populations

The global prevalence of type 2 diabetes (T2D) is increasing, with sub-Saharan Africa most affected. Although the development of T2D differs between African and European populations, and between men and women, risk screening and guidelines for the prevention of T2D are generic. This collaboration between Sweden, Germany and South Africa enables the measurement of circulating proteins and metabolites to identify sex- and ethnic-specific biomarkers for the early prediction of T2D risk in two African cohorts (South African and Ghana) and a European (Swedish) cohort. We will also link these biomarkers to dietary patterns, which will be used to inform targeted dietary modifications for primary prevention of T2D in the different populations. The cost effectiveness of the targeted dietary modifications, as well as the perceptions among target populations regarding these early preventative strategies will be assessed in the respective countries to inform future implementation of personalised prevention strategies.

Omics Approach for Personalized Prevention of Type 2 Diabetes Mellitus for African and European Populations (OPTIMA)
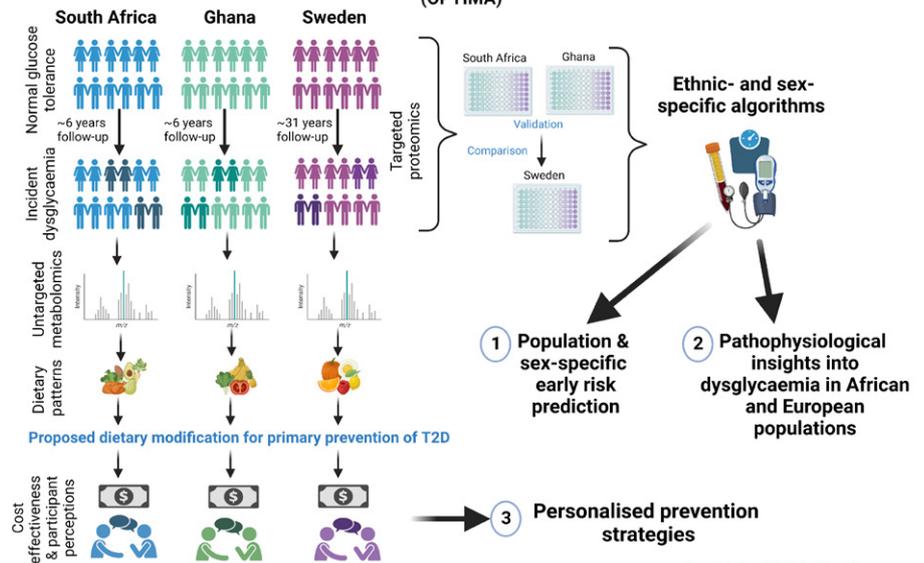
Created with BioRender.com.

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OVA-PDM

Personalising the clinical decision making in ovarian cancer through patient-derived in vitro models

High-grade serous ovarian cancer (HGSOC) is a difficult-to-treat disease, mainly due to the lack of treatments for preventing tumour relapse following the primary surgery. In the last few years, a new class of compounds termed PARP inhibitors (PARPi) have emerged as highly promising drugs that prolong dramatically the relapse-free interval in HGSOC patients. Because of their mechanism of action, PARPi are currently given to a subgroup of patients whose cancer is defective in a specific mechanism of DNA repair. However, even within this subgroup there are patients who fail to respond, while, on the other hand, a significant fraction of patients, who are not identified as DNA repair-defective, do show very good response. Unfortunately, at the moment we have no means to identify in advance patients who are likely to benefit from PARPi and, hence, could receive a personalised treatment. Our consortium will implement innovative, patient-derived experimental models and cutting-edge technologies to design novel tools for the prediction of PARPi response, thus helping to tailor the therapies and to defeat HGSOC recurrence.
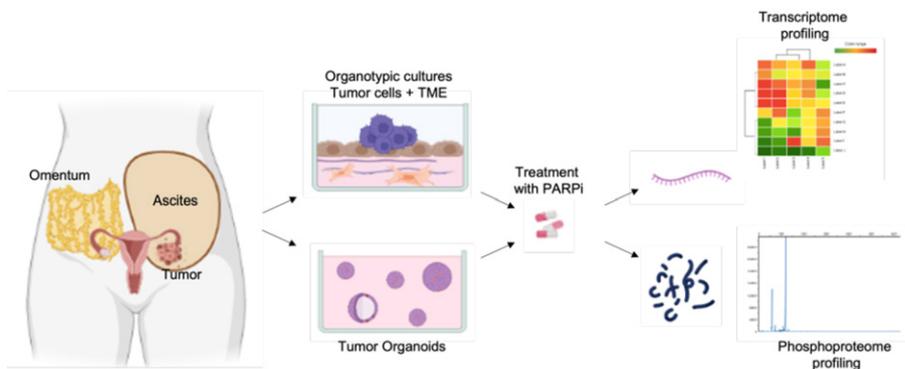
Schematic representation of the workflow for the identification of predictive biomarkers for PARP1 response.
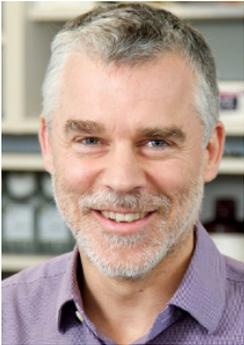
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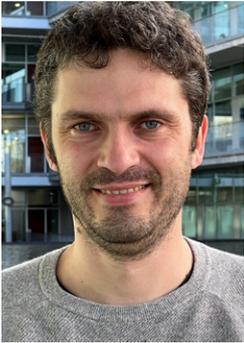
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PARADISE
PersonAlisation of RelApse risk in autoimmune DISEase

Autoimmune disease affects 10% of adults, most of whom are women, and two of the top five medications with the highest cost globally are used to keep these recurring conditions in remission. These medications suppress the immune system, leaving the patient exposed to increased infection and cancer risk. The PARADISE consortium patient groups have highlighted this issue and the uncertainty about future relapse as a key research agenda. Therefore, we aim to **develop a personalised prediction tool that accurately defines the patient's risk of disease recurrenc**e so that medication doses can be tailored and, in some cases, stopped safely. We use **systemic vasculitis** as a typical autoimmune disease, bringing together clinical, biomarker and smartphone derived wellbeing data to inform predictive algorithms underpinning a physician tool. Such artificial intelligence (AI) applications are coming under intense EU scrutiny, so we will co-develop an "**AI transparency notice**", which will make explicit and explainable the PARADISE tool clinical outputs.

PersonAlisation of RelApse risk in autoimmune DISEase - *PARADISE*
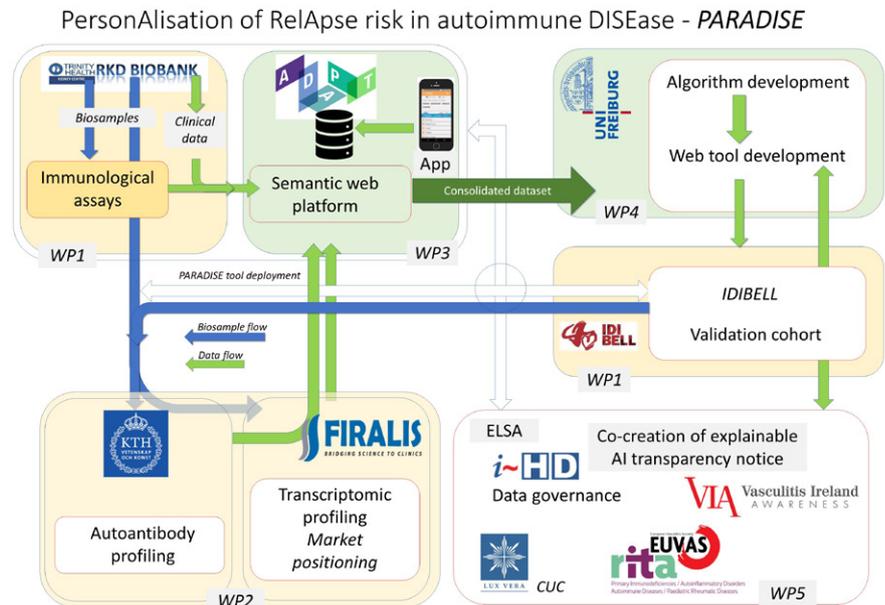
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PERMANENS

Towards personalised clinical management of suicide risk through data-driven clinical decision support using transnational electronic registry data

Suicide is a major, yet preventable, public health issue, representing an annual loss of 34.6 million years of life worldwide. Clinical management of patients with suicide risk is a challenging task, in part because suicide represents highly complex difficult-to-predict behaviour. The PERMANENS project will develop a prototype of a Clinical Decision Support System (CDSS), i.e., a medical software programme that assists clinicians in the personalised management of suicide risk. Using machine learning-based algorithms, the CDSS will enable accurate suicide risk prediction and the subsequent personalised allocation of evidence-based treatment. Data for the project will be obtained from population-representative electronic registries from Ireland, Norway, Sweden, and Catalonia (Spain). To maximize its clinical usefulness, the CDSS prototype will be co-created with both patients and clinicians through user-oriented qualitative implementation research.
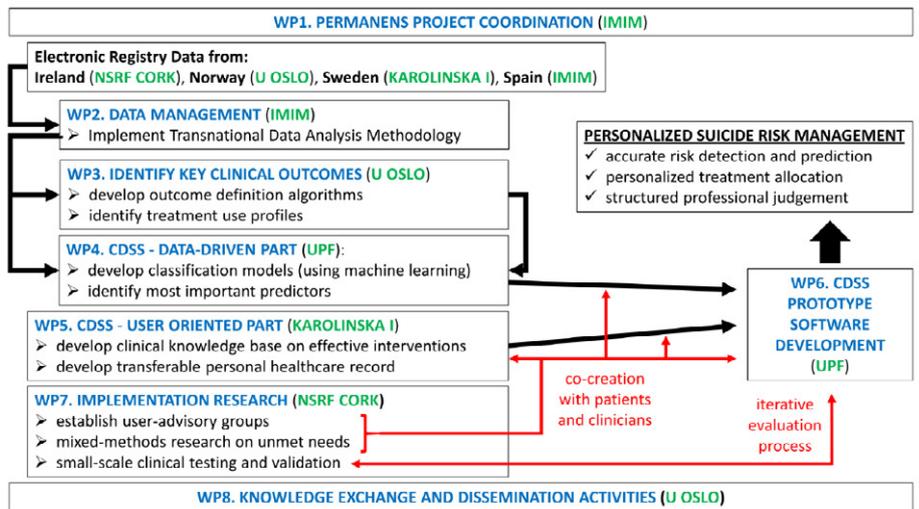
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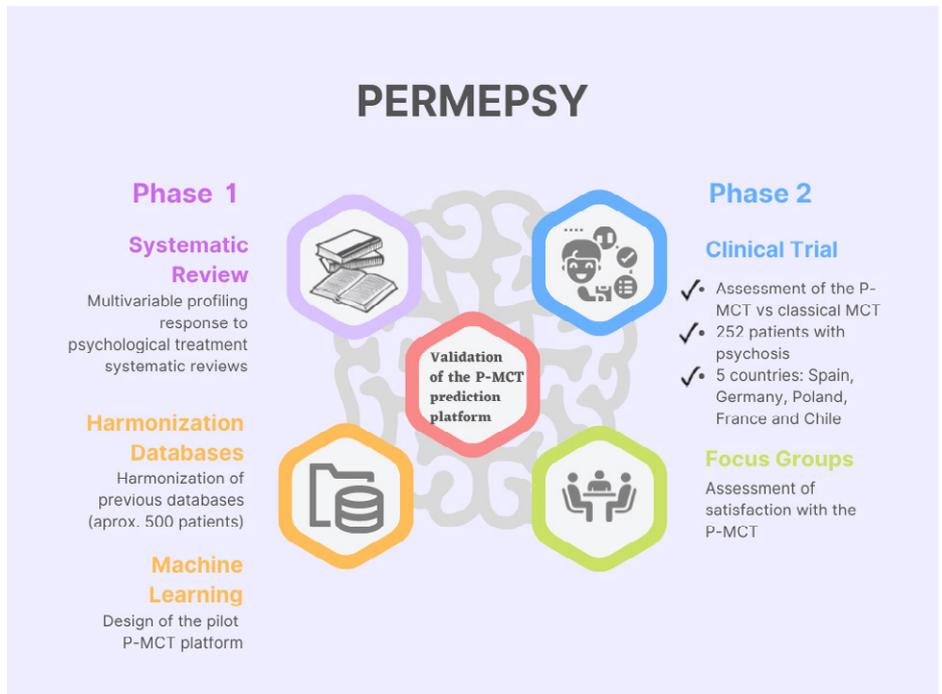🇵🇱 Lukasz Gaweda, Polish Academy of Sciences (PAoS), Poland

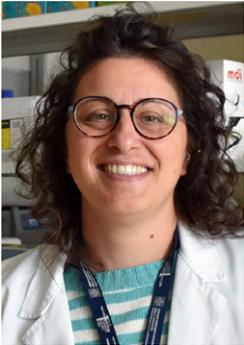🇪🇸 Caroline König, Universitat Politècnica de Catalunya (UPC), Spain

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PERMEPSY

Towards a personalised medicine approach to psychological treatment for psychosis

Despite the efficacy of psychological interventions in people with psychosis few patients receive them, and none of them were personalised. PERMEPSY aims to integrate new technologies such as harmonisation of data and machine learning for providing a prototype platform that will allow to personalise a psychological treatment named Metacognitive Training (MCT). The project is divided into two phases. The first one consists of a systematic review of the literature and the harmonisation of previous data (aprox. 500 patients with sociodemographic, clinical, cognitive and meta-cognitive, and biomarkers information) to develop a prototype platform that will predict personalised treatment (P-MCT). The second phase will validate the P-MCT compared with classical MCT in a prospective pilot clinical trial study in 5 countries: Poland, Germany, France, Chile and Spain (including 252 patients). PERMEPSY project will develop an open platform for clinicians to predict the response to MCT and recommend a personalised MCT treatment.

PERMEPSY

Phase 1

Systematic Review
Multivariable profiling response to psychological treatment systematic reviews

Harmonization Databases
Harmonization of previous databases (aprox. 500 patients)

Machine Learning
Design of the pilot P-MCT platform

Validation of the P-MCT prediction platform

Phase 2

Clinical Trial
✓ Assessment of the P-MCT vs classical MCT
✓ 252 patients with psychosis
✓ 5 countries: Spain, Germany, Poland, France and Chile

Focus Groups
Assessment of satisfaction with the P-MCT

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PORTRAIT
A multi-omic stratification and a non-invasive tool for early recognition of triple negative and Her2+ breast cancer patients responders to neoadjuvant therapy

Neoadjuvant therapy (NAT) is the standard initial treatment for Triple Negative and Her2+ breast cancers. The tumour response to NAT diverges widely due to the influence of several individual factors, including microbiota, that have a crucial role in immune response and in conditioning molecular pathways. Thus, a systematic and integrated stratification of the patients at the onset of the disease, together with the evaluation of the common decision-making criteria, will help to recognise responders and improve patient care and quality of life. **PORTRAIT** aims to create a **multidimensional ID** of responders and non-responders to NAT integrating host characteristics and clinical data with tissue and distal microbiota characteristics (gut and skin microbiota) to detect the individual panel of determinants affecting the therapeutic outcome by a multiomic approach. It also aims to create a **non-invasive predictive tool** based on **volatilomics** and **test personalised therapy approaches in 3D models**.
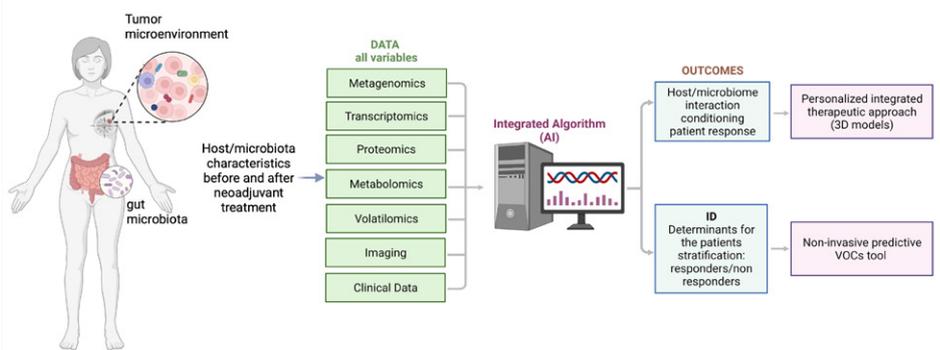
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RELIABLE

Targeting subclinical motor and cognitive impairment in patients with early onset Multiple Sclerosis at high Risk of disEase activity through a preventive personaLised and InnovAtive rehaBiLitation stratEgy

Prevention of progression from the earliest stages of the disease is an important unmet need in Multiple Sclerosis (MS). In this study we will focus on a comprehensive assessment of subclinical deficits in patients without clear evidence of neurological dysfunction. Applying personalised interventions targeted to the patient's deficits may reduce the burden of these deficits, improve the patient's quality of life and possibly reduce the chance of future, clinically evident, disability accrual. The aim of this pilot study is to assess the subclinical burden of neurological impairments in early Relapsing-Remitting MS patients with no evident neurological disability by applying a comprehensive evaluation, including comorbidities, lifestyle, imaging data, neuropsychological evaluation, gait and balance analyses. From these analyses, we will obtain a risk score for disability worsening over the short-term (1 year). We will then evaluate in a validation cohort the reduction of the rate of patients with evidence of disease activity using a comprehensive and personalised approach (lifestyle counselling, advanced motor and cognitive rehabilitation). As an added value, we will take into account patient preferences and values to support tailoring the interventions.
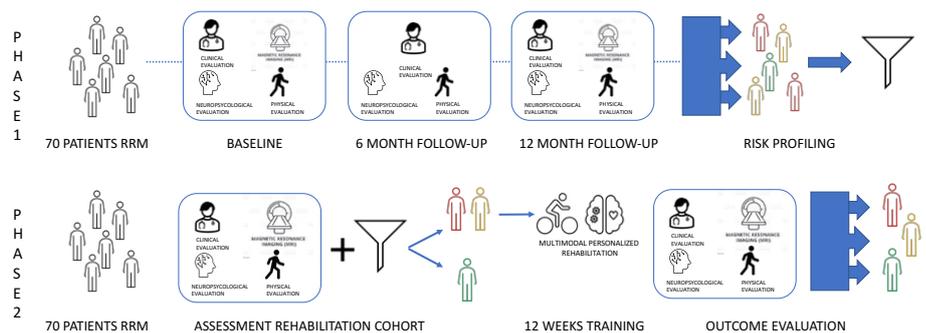
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SIGNAL
Body fluid proteome SIGnatures for persoNALised intervention to prevent cardiovascular and renal complications in diabetes

Diabetes and the associated cardiovascular and renal complications are among the largest burdens for patients, as well as the public healthcare system. Several different drugs that show a significant benefit are available, with the largest benefit produced if given at the earliest possible time point. However, guidance on which specific medication to apply per patient is currently lacking. Partners in this consortium have investigated urine and plasma proteome in multiple clinical studies and identified several biomarkers expected to predict drug response. In addition, the consortium has access to large biobanks of diabetic patients undergoing different types of pharmacological intervention. Building on these extensive available resources, SIGNAL targets to evaluate and establish predictive biomarkers that enable guiding anti-diabetic treatment with respect to prevention of chronic kidney and cardiovascular disease. The study will establish and prompt advancement towards clinical implementation of predictive biomarkers-opening the way towards the personalised treatment of people with diabetes.

![ERA PerMed]
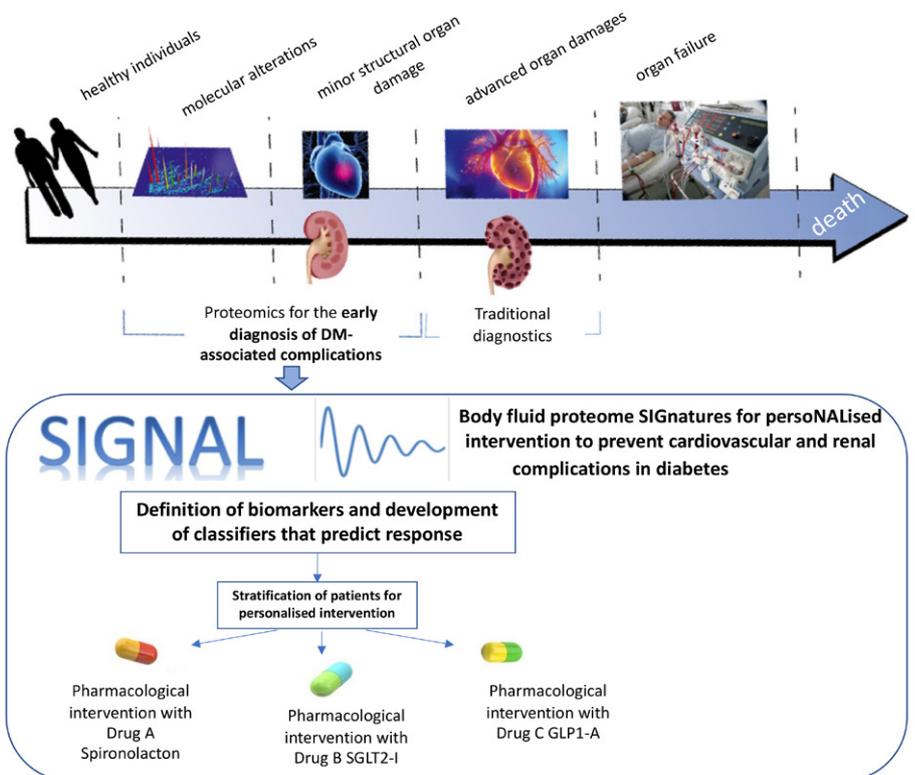
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SpareKid
Multi-markers risk assessment of kidney sensitivity to injury to personalise prevention of acute kidney injury

Acute kidney injury (AKI) is an extremely complex life-threatening disease with high mortality and chronic kidney/non-kidney consequences. AKI is characterised by (1) the (current) inability to predict its development before the insult, even in well-controlled and frequent clinical settings such as cardiac surgery or chemotherapy, and (2) the huge heterogeneity of the kidney response even after an insult of similar intensity. The aim of SpareKid is to better predict the development of AKI to allow dedicated primary prevention and reduce its costs. The innovative concept of SpareKid is to define a so-called non-invasive Kidney Resilience Index (KRI), modeling AKI as a maladaptive kidney response to the insult. The KRI will be defined based on in-depth and multiscale molecular and clinical data using a holistic big data-based strategy to integrate high throughput urinary and plasma proteomic, immunologic mRNA and cell population signatures, genetic whole genome sequencing (WGS) signatures and detailed clinical parameters to optimally model the complexity of AKI. Last, using data from the National Systems of Health, we will model the cost-effectiveness of the KRI to determine the cost sparing of a preventive strategy.

The SpareKid Project
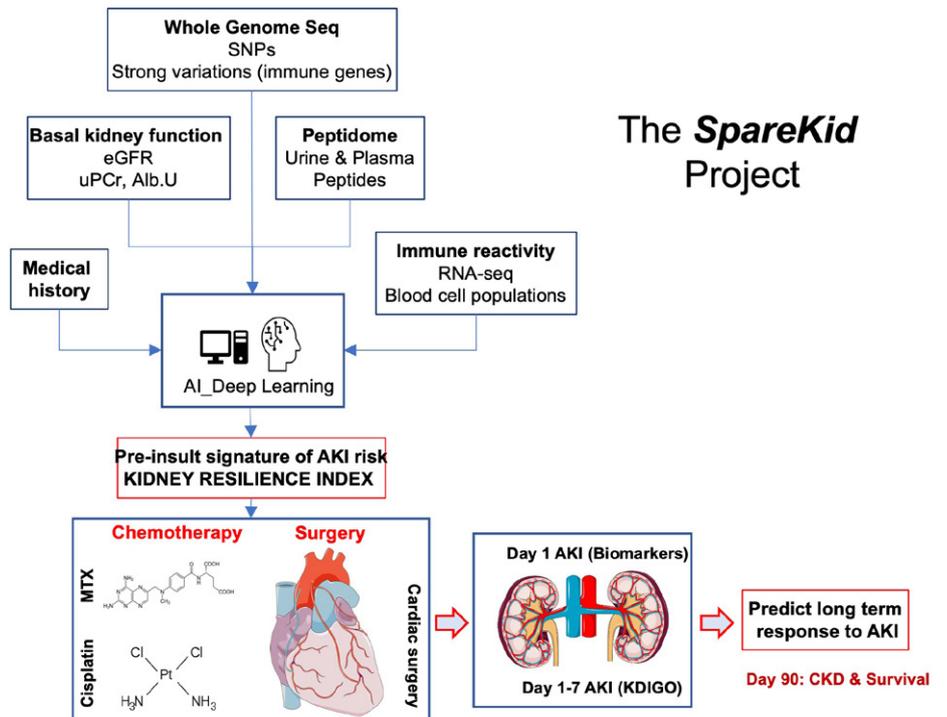
Cost-effectiveness of the **Kidney Resilience Index**

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Stracyfic

Patient Stratification by Standardization of the Image-based Sweat Test for Cystic Fibrosis for use in Clinical Routine

The demonstration of a salty sweat has long been used to diagnose cystic fibrosis (CF), a rare disorder affecting 1 in 2,500 live births and associated with high morbidity and mortality. CF is caused by mutations resulting in a loss-of-function of the CFTR protein that mainly acts as a chloride channel. It leads to dramatic trans-epithelial ion and water transport abnormalities and produces a thick mucus obstructing airways and duct lumens of exocrine glands. Beyond complex treatments, mainly symptomatic, CFTR modulators have recently been developed to mitigate the mutation effects; there is, however, still no cure for CF. Moreover, there is an unmet need of validated biomarkers of CFTR function to quantify the remaining CFTR activity, e.g. to classify the level of the base defect and later assess the efficacy of target therapies. We aim at developing a usable common standard for the required experiments, the automated analysis via software and providing the experimental hardware setups for an easy dissemination of the technique to other sites.

Stracyfic will offer a novel strategy to better classify and monitor patients by their individual level of the disease-causing effect. Enabling better detection as well as better management of the disease in the long run.
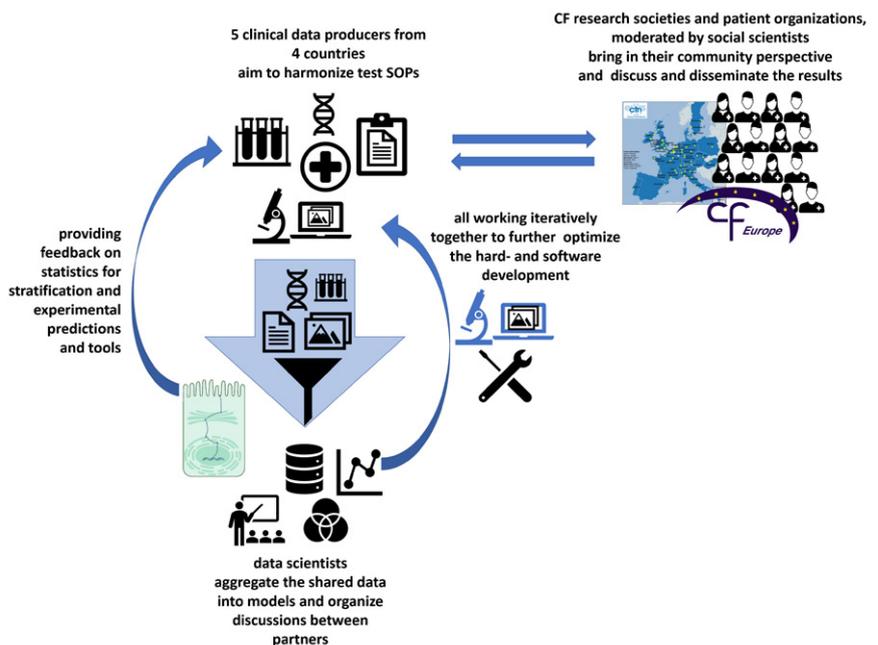
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UBIOBCA
Urine biomarkers for bladder cancer diagnosis and surveillance: a multicentric study to assess the diagnostic accuracy of a comprehensive diagnostic tool

Bladder cancer (BC) ranks as the tenth most prevalent cancer in the world (IARC, WHO), with a steady rise in its incidence and prevalence, and is accompanied by a high morbidity and mortality. The current standard of care to diagnose bladder cancer is cystoscopy, which consists of inserting a camera in the urinary track to the bladder. Although the detection rate is high, the technique/equipment is expensive, invasive, unavailable worldwide, and, most importantly, uncomfortable and associated with risk of complications. Therefore, there is a critical need to establish a non-invasive, low cost, and sensitive method for the early detection and monitoring of BC. In this project, we aim to investigate the robustness of using urine biomarkers as a diagnostic tool in different populations through a large international multicentre study (Canada, France, Germany). This would demonstrate the applicability of such tests to be used as universal non-invasive biomarkers for early detection and surveillance of BC in different populations to reduce the number of procedures, improve the patients' quality of life and lower the costs.
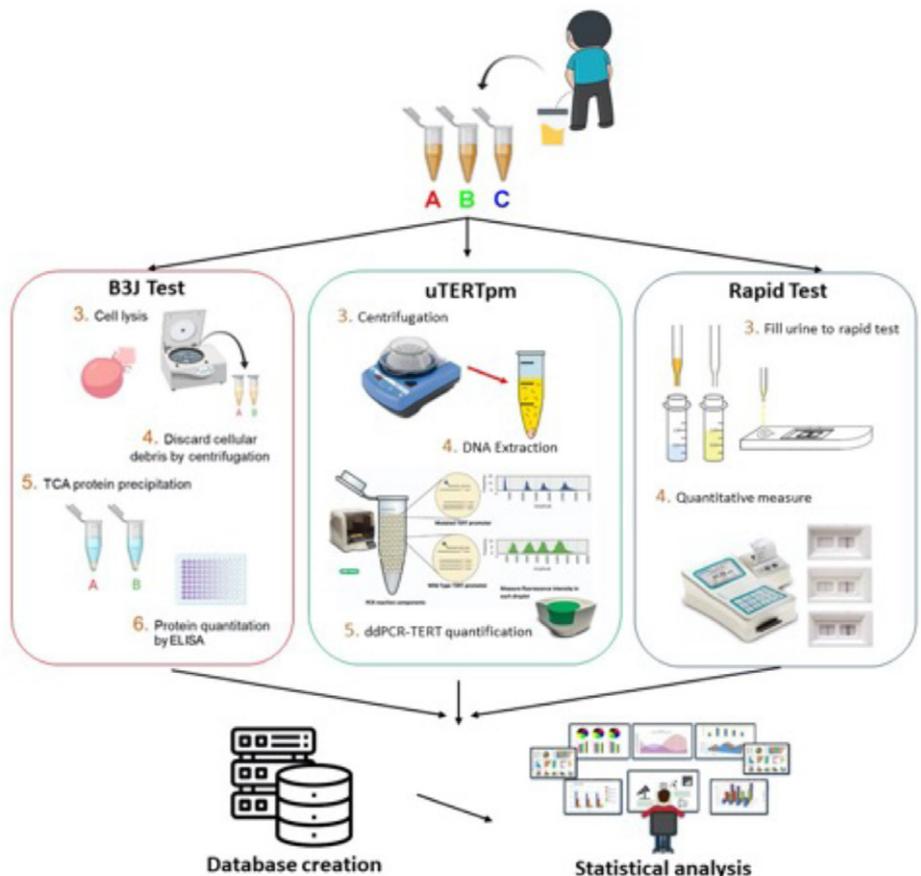
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UriCoV
URInary peptidomic patterns of Long-COVID syndrome

Post acute sequelae of SARS-CoV-2 infection (PASC), also referred to as long COVID, is the most frequent, yet poorly characterised sequelae of COVID-19. It has tremendous, unpredictable consequences on personal health and socioeconomic status of affected individuals, and on global economic issues. UriCov is a multidisciplinary, comprehensive project with the aim to investigate in depth the molecular phenotype(s) of individual patients previously infected by SARS-CoV-2 and identify patients at risk of PASC. This will be achieved through multi-disciplinary research based on omics and clinical data in a bioinformatics framework, based on the hypothesis that endothelial damage is a key event in PASC. The developed molecular tools may allow patient stratification to initiate personalised treatment for prevention of PASC prior to symptoms and to decrease the PASC incidence. UriCoV will also provide missing fundamental knowledge on the molecular pathophysiology of PASC.

Urinary peptidomics of post acute sequelae of SARS-CoV-2 infection (PASC)