



NEWSLETTER 5

January 2021

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 2020

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

18 successful consortia are funded with a total investment
of more than 23.3 million Euros for three years



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ERAPerMed 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.

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LOOKING BACK AT 2020 AND INTO THE FUTURE

This past year has been a challenging one for each and every one of us worldwide. It required flexibility and adaptability, as well as tolerance and patience both at home and in the work space, especially since the two have become inseparable. We, at ERA PerMed, did not let the circumstances slow us down. In this past year, 2020, we have executed our 3rd call for proposals, JTC2020, of which you can read about in more details in this newsletter, we have collaborated with ICPeMed on preparing the draft document on the future European Partnership on Personalised Medicine (EP PerMed) and announced a 4th call for proposals, JTC2021, which is now open for applications!

Since ERA PerMed is not alone in the European personalised medicine ecosystem, we would like to acquaint you with two new initiatives in the PerMed field. A new Coordination and Support Action (CSA) - The EU-Africa PerMed project is expected to begin in 2021, with the final objective of integrating African countries into ICPeMed activities as a means to contribute to the implementation of PerMed in the global context, fostering joint PerMed projects and programmes between Europe and Africa and strengthening bilateral EU-Africa science, technology and innovation in health. The second initiative has already taken off - PerMedCoE - coordinated by the Barcelona Supercomputing Center and funded by the European Commission, this recently launched High-Performance Computing (HPC) centre of excellence will optimise codes for cell-level simulations in HPC/Exascale and bridge the gap between organ and molecular simulations, thus contributing to the European Personalised Medicine Roadmap.

With that, we wish you all health, excellent research, fruitful collaborations and great advancements in promoting personalised medicine worldwide this New Year 2021!

Announcements

ERA PerMed Joint Transnational Call 2021!

“Multidisciplinary Research Projects on Personalised Medicine – Development of Clinical Support Tools for Personalised Medicine Implementation”

Submission deadline for pre-proposals: March 4th, 2021 [Click for details](#)
 Info day for potential applicants: January 25th, 2021 (13:00 CET) [Register here](#)

COMING UP SOON!

2nd ICPeMed conference ‘Personalised Medicine – From Vision to Practice’

25-26 February 2021
[Virtual conference](#)

INTRODUCING

PerMedCoE: Exascale-ready cell-level simulations for European Personalised Medicine

[Click for details](#)

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Joint Transnational Call for Proposals 2020: “MULTIDISCIPLINARY RESEARCH PROJECTS ON PERSONALISED MEDICINE – PRE-/ CLINICAL RESEARCH, BIG DATA AND ICT, IMPLEMENTATION AND USER’S PERSPECTIVE”

To align national research strategies, promote excellence, reinforce the competitiveness of European players in Personalised Medicine (PerMed), and enhance the European collaboration with non-EU countries, 31 funding organisations from 23 countries agreed to launch the third ERA PerMed Joint Transnational Call (JTC) for collaborative innovative research projects in PerMed. With the Joint Transnational Call for Proposals 2020 on “Multidisciplinary Research Projects on Personalised Medicine – Pre-/Clinical research, Big Data and ICT, Implementation and User’s Perspective”, ERA PerMed aims 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 PerMed into clinical practice and on ethical, legal and social implications across the participating countries and beyond.

A new funding organisation, which was not part of previous ERA PerMed Calls, joined the JTC2020: The National Secretariat for Science, Technology and Innovation of Panama (SENACYT), Panama.


188 eligible pre-proposals were submitted, 56 consortia were invited to submit a full-proposal and **18 proposals with a total funding amount of 23,267,591€ will be funded!**





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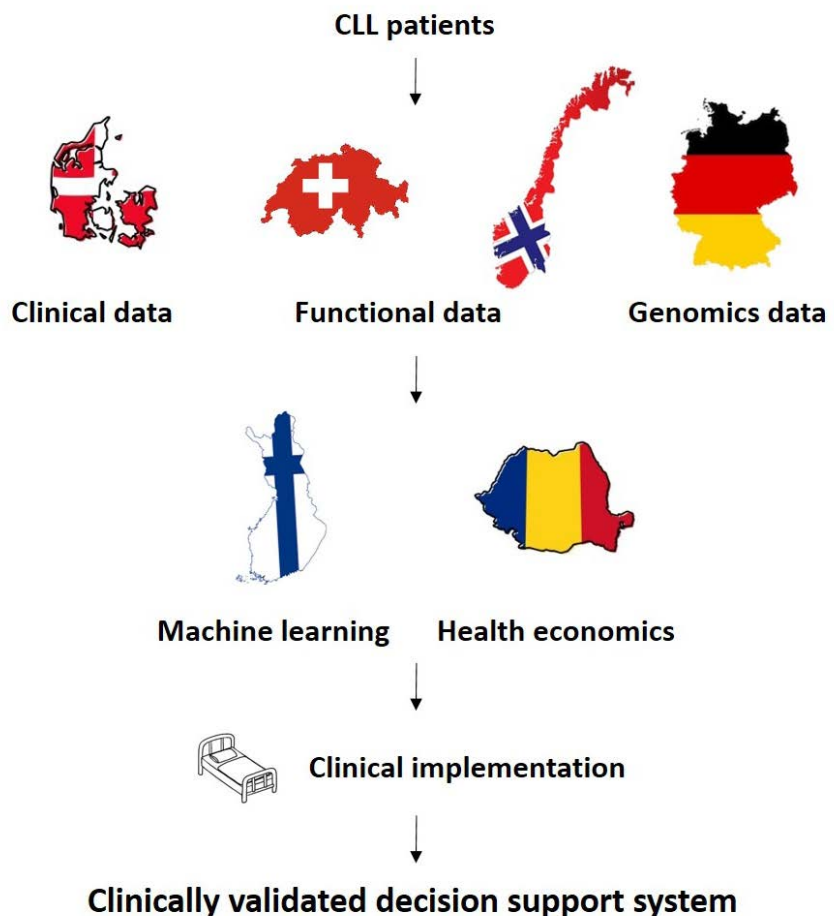
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CLL-CLUE

Tailoring the targeted treatment of chronic lymphocytic leukemia


Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in Europe and it remains incurable. Targeted therapies have revolutionized the treatment of CLL. However, many patients develop resistance, have severe side effects or relapse during treatment. There is an unmet medical need for tailoring optimal therapy for each patient in order to prevent ineffective treatment and toxic side effects. The CLL-CLUE project will identify multi-omics biomarker panels and implement artificial intelligence-based clinical decision support systems to guide personalised treatment decisions. We expect that this will lead to significantly increased treatment efficacy, individualisation of therapy and reduced drug use and side effects. In addition, reduced consumption of drugs and cost-effective outcomes will lower financial stress that the health care providers and patients experience.





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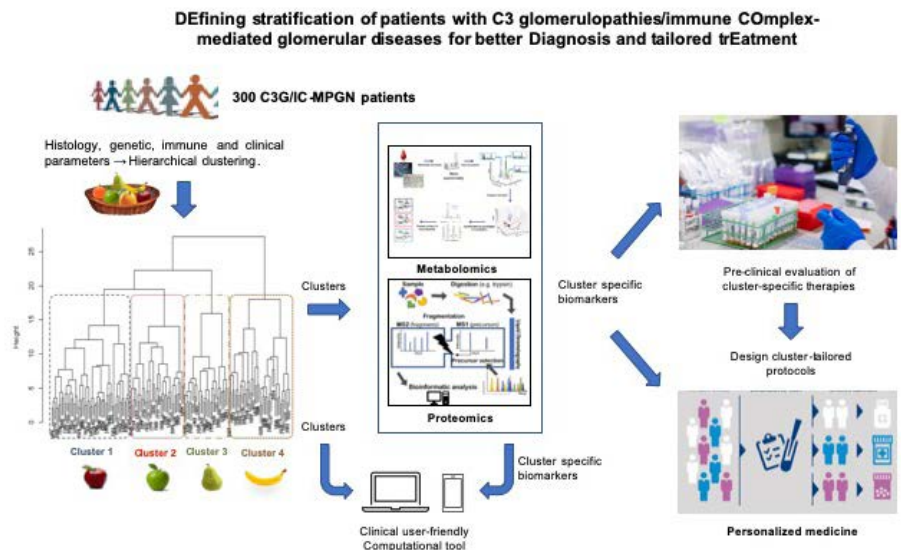
 Isabelle Budin Ljosne, Norwegian Institute of Public Health, Norway

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DECODE

DEfining stratification of patients with C3 glomerulopathies/ immune COmplex-mediated Glomerular diseases for better Diagnosis and tailored treatment


Primary membranoproliferative glomerulonephritis (MPGN) represents a group of rare kidney disorders associated with complement activation. There is no specific therapy and the prognosis is unfavorable: about half of all patients, mostly children, develop end-stage renal disease and need dialysis within 10 years of onset. MPGN is heterogeneous and patients have abnormal activation at different levels of the complement system. Several drugs targeting complement have been already approved or are investigated in trials for other conditions. However, trials to test new therapeutics will be heavily influenced by the heterogeneity of MPGN. The current classification into C3 glomerulopathy (C3G) and immunecomplex-mediated MPGN (IC-MPGN) based on only histological data, does not reflect the etiology and is inefficient. Thus, there is an obligation in future trials to ensure that each patient is maximally characterised in order to receive the right drug. Previous studies identified four patient clusters, instrumental to define early and late complement activation. DECODE will implement this strategy by combining omics approaches (i.e. WES, proteomics and metabolomics) and hierarchical clustering analysis to define a precise stratification of patients with C3G/IC-MPGN, and to identify specific biomarkers, which will be instrumental for diagnosis, predicting prognosis and tailoring the right therapeutic strategy for the right patients.





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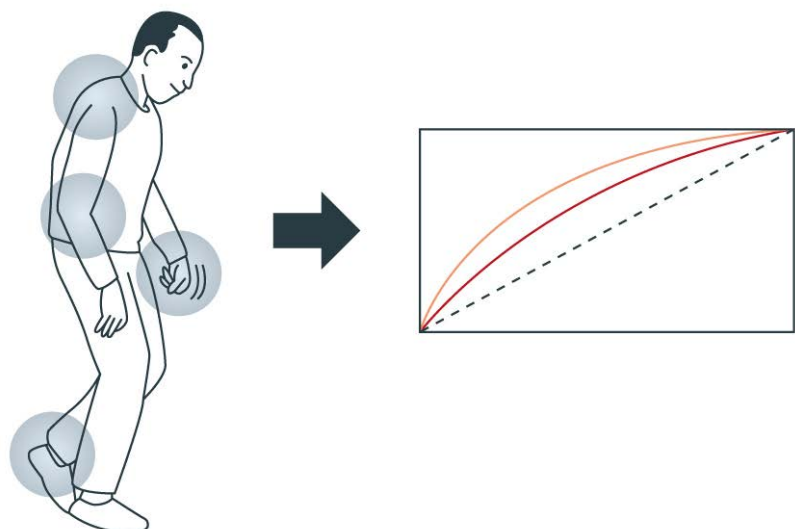
DIGIPD

Validating DIGItal biomarkers for better personalised treatment of Parkinson’s Disease

Parkinson’s Disease (PD) is affecting 7-10 million patients worldwide with strongly increasing prevalence in Western societies. Patients suffer from a variety of symptoms (e.g. tremor, gait and speech impairment, cognitive decline), which differ widely between individuals and can also vary over short periods of time. The cause of the disease is mostly unknown. Existing medications cannot stop disease progression, which highly varies from subject to subject, imposing major challenges for disease management as well as discovery of new medications.

DIGIPD evaluates modern digital technology measuring impairment of gait, voice and face movement with respect to more accurate diagnosis of symptoms (also outside clinics) and to prediction of disease progression. DIGIPD will disentangle the relationship of digital measures to established clinical questionnaires and to molecular biomarkers. The outcome of DIGIPD could be used by physicians to adapt treatment. Moreover, pharmaceutical companies can use a grouping into similar progressing patients to increase the chances of clinical trials bringing new and better drugs to the market.


Since DIGIPD heavily relies on Artificial Intelligence using personal data, the project will include an analysis of the legal situation, and it will involve patients via dedicated interviews.





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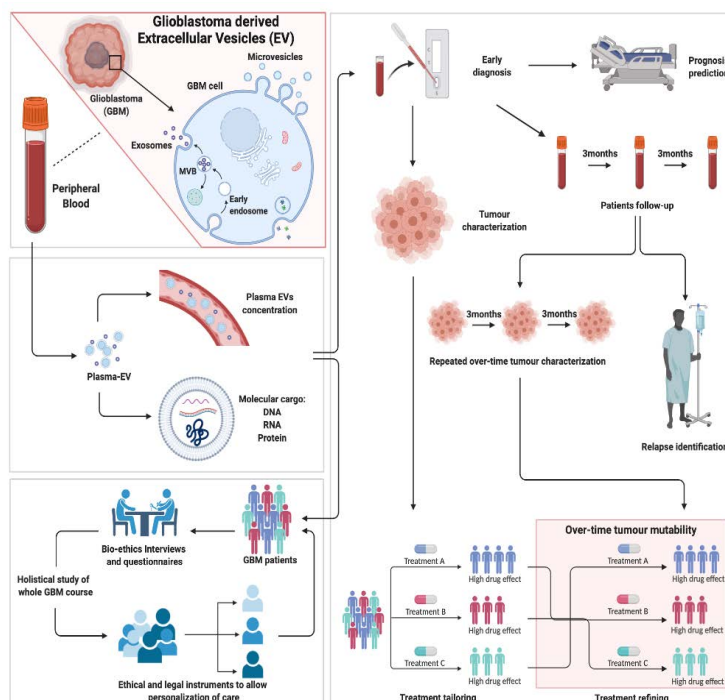
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EV-glio

Plasma extracellular vesicles (EVs): the key for precision medicine in Glioblastoma


The project aims at revolutionising the treatment of glioblastoma, the most lethal tumour of the central nervous system, through a consistent implementation of personalised medicine. Currently available GBM management is standardised and non-curative, as it can only increase patients survival by a few months. Personalised care relies on the characterisation of the heterogeneity of glioblastomas in a close and reliable way, tailoring and adjusting the treatment continuously to overcome the tumour mechanisms of defence that by the time invariably arise. The project focuses on the potential of extracellular vesicle-based liquid biopsy, with the goal to validate the extracellular vesicles as a diagnostic and prognostic biomarker, and as a follow-up tool, able to cope with the heterogeneity and mutability typical of glioblastomas. By proposing a multi-level characterisation of all the informative power of these blood-derived vesicles, the project will analyse plasma extracellular vesicles concentration and molecular cargo (DNA, RNA, protein) during the whole disease course. In parallel, the project envisages a line of bioethical research where each patient is longitudinally followed for the entire history of his disease, in order to develop ethical tools to optimally implement the principles of personalised medicine in the treatment of glioblastomas and create the basis for potential applications in other cancers.





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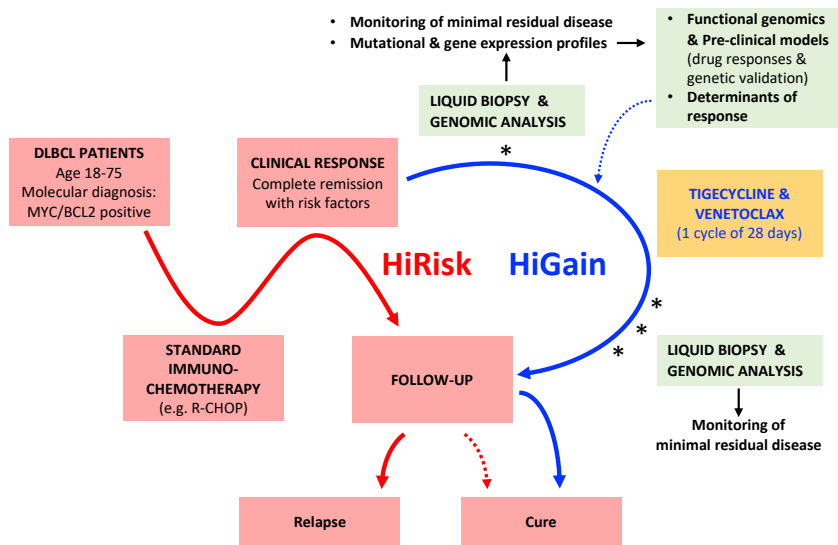
HiRisk-HiGain

Rethinking personalised cancer therapy: targeting minimal residual disease in high-risk lymphoma patients

Diffuse Large B-cell lymphoma (DLBCL), a cancer arising from B-lymphocytes, is currently treated by immuno-chemotherapy, which cures about 60% of the patients, while others eventually relapse. Resistance to therapy results from cancer-associated mutations that are variable from patient to patient - utilizing those features to guide tailored therapeutic approaches is the essence of personalised medicine.

A particularly high-risk scenario in DLBCL is the co-activation of two cancer-promoting genes, MYC and BCL2, resulting in so-called “double-hit” lymphomas. We previously reported that in animal models these tumours can be eradicated by the combination of two drugs, Venetoclax and Tigecycline. Here, we will use an innovative personalised scheme to translate those findings into the clinic.

Following an initial response to standard treatment, patients will receive Venetoclax and Tigecycline to eradicate residual disease, thus averting relapse. Blood samples will be collected at each step and subjected to genomic analyses, allowing to detect even rare tumour cells and map their mutation profiles. Hence, we shall not only assess the efficacy of the drug combination in the clinic, but also decipher the molecular features that distinguish responders from non-responders, thus guiding the introduction of this new personalised therapy in routine healthcare.




The **HiRisk-HiGain** trial will address whether complementation of standard immuno-chemotherapy (red line) by a consolidation treatment with Tigecycline and Venetoclax increases the frequency of disease eradication – i.e. cure – in MYC/BCL2-associated diffuse large-B cell lymphoma (DLBCL). Patients will be enrolled based on positivity for MYC and BCL2 (with either IHC or FISH) and the achievement of primary remission with remaining risk factors (slow responders or detectable minimal residual disease), and will include a subset of «double-hit» cases with dual translocations. Repeated liquid biopsy (blood sampling) and monitoring of minimal residual disease shall allow to anticipate eventual relapse and to unravel the genetic correlates (or biomarkers) of treatment response. Complementary experiments in pre-clinical models (mice) shall validate those biomarkers and highlight the mechanisms connecting them to treatment response.



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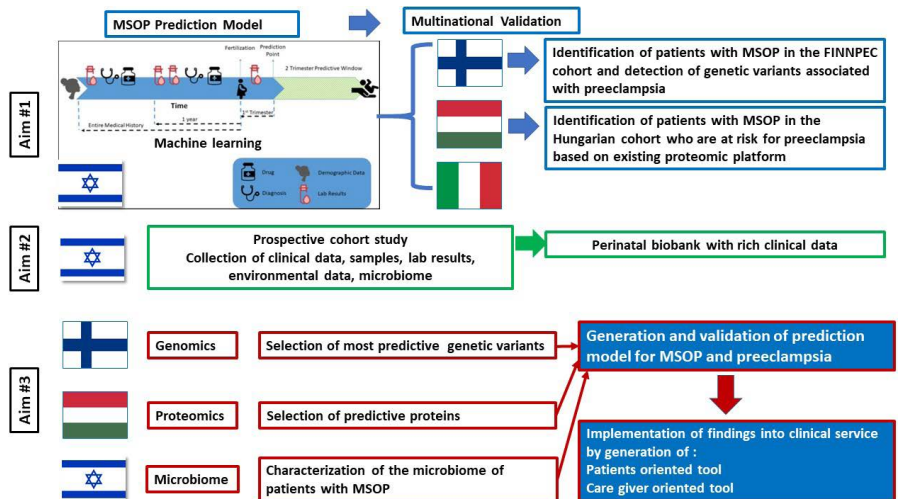
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 Hannele Laivuori, Clinical Medicine, Faculty of Medicine and Health Technology, Tampere University, Finland

MSOP-PRE

Early PREDiction and personalised PREvention of Metabolic Syndrome Of Pregnancy and PREeclampsia


Metabolic syndrome of pregnancy (MSOP) affects 15-20% of women. This syndrome is related to pregnancy complications, including preeclampsia, diabetes and pre-term birth. In the current proposal, we will generate personalised prediction models for MSOP and its gestational complications. To accomplish these aims, we will characterise MSOP and its complications by the clinical and epidemiological information collected in Soroka Medical Center, including hospital and HMO medical records for >300,000 deliveries (Israel), life-style habits and lab results. Subsequently, we will validate the prediction model in the European participating centers (Italy, Hungary and Finland), and identify candidate genes (Finland) and proteins (Hungary) for further analysis. In Phase II, we will recruit a prospective clinical cohort of 1700 pregnant women, administer a questionnaire on life style and dietary factors, and collect samples for further genome, proteome, microbiome and exposome analysis (air pollution and meteorology). This information will be incorporated in a multimodal 'systems medicine' approach, to detect personal modifiable risk factors of MSOP. The knowledge on these risk factors early during gestation will enable development of appropriate interventions and thus improve maternal and neonatal health and impact their long-term quality of life.





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ONCOLOGICS

Computational modelling and functional validation platform for personalised colorectal cancer clinical therapy decision support


The ONCOLOGICS consortium is launched with the goal of bringing Personalised Medicine to the clinic. The idea is to predict the response of each individual tumour to therapy based on a platform combining in silico modelling with functional validation using patient-derived ex vivo cultured tumour tissues. This approach aims to move away from a 'one size fits all' approach to identify individual therapies based on the unique genotypic and phenotypic characteristics of each tumour. Our ex vivo platforms, patient-derived tumour organoids and spheroid cultures, allow for a full systems medicine approach encompassing iterative cycles of computer model revision informed by ex vivo experiments, and targeted follow-up experiments guided by model predictions. Experimental readouts include patient cancer cell viability data as well as specific molecular readouts that report on cancer cell growth signaling. Ultimately, model predictions are tested against observed cancer patient therapy responses. The in silico and ex vivo platforms jointly pave the way for future 'functional personalised medicine'. ONCOLOGICS represents a continuation and extension of the ERACoSysMed project COLOSYS and fits under the umbrella of the DrugLogics initiative that applies Systems Medicine approaches for therapy design.

The infographic features a central map of Europe with colored pins indicating the locations of the project partners. Above the map, a circular diagram shows the 'COORDINATOR' (Åsmund Flobak) and the 'Project Management Team' (TTO) with arrows indicating collaboration. Below the map, a row of circular portraits identifies the team members: WP1 IC, WP2 NTNU, WP3 BSC, WP4 UU, P2 Charité, and P5 ProtAtOnce. A text box on the left describes the project as a 'Computational modelling and functional validation platform for personalised CRC clinical therapy decision support'. The bottom right corner contains the ERA PerMed logo, the project title 'ONCOLOGICS', and the full project title: 'Computational modelling and functional validation platform for personalised colorectal cancer clinical therapy decision support'. It also lists the project ID 'ERAPERMED2020-036' and the acronym 'ONCOLOGICS'.



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OptiCAN

Optimized T cells for personalised immunotherapy of solid CANcer entities

The overall goal of OptiCAN is to overcome the present limitations of CAR T cell therapies and extend their application towards personalised immunotherapy of solid tumors through advanced genetic engineering of patient-derived T cells.

We will achieve this goal by testing different innovative approaches for functional improvement of T cells to treat pancreatic cancer and melanoma as model indications. In more detail, we will

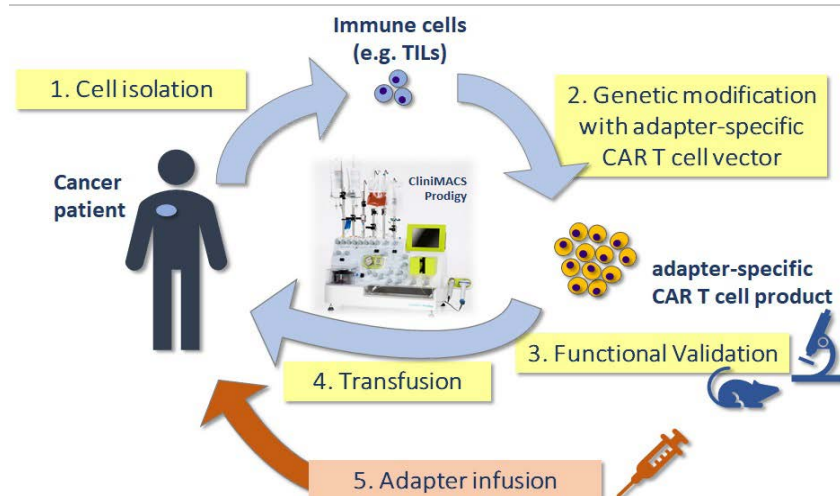
- > develop most effective gene-engineering technologies for functional improvement of the CAR T cell product by use of innovative adapter-CAR and boost-CAR technologies

- > apply advanced imaging technologies to investigate the tumor microenvironment and to develop strategies for overcoming its immunosuppressive milieu

- > establish innovative preclinical animal models (PDXv2.0) to prove the in vivo efficacy of the generated T cells

- > integrate the project achievements into a novel manufacturing workflow for optimised personalised cell products

We will additionally investigate ethical and regulatory aspects currently slowing down the transition of personalised cancer immunotherapy into clinical routine. Our innovative treatment strategy relying on highly effective and controllable CAR T cell products can easily be transferred and spread to hospitals across Europe. Thus, we will finally improve the perspectives for terminally-ill cancer patients having no further alternative treatment options.




OptiCAN therapeutic strategy. Tumor reactive T cells are isolated from the patient (1), expanded and genetically modified with an adapter-specific CAR T cell construct (2). Functional validation through advanced imaging and preclinical animal models (3). Automated manufacturing takes place in the CliniMACS Prodigy device. After 7-14 days the CAR T cell product is transfused back into the patient (4) and the adapter molecule is infused separately to in vivo "arm" the CAR T cells and promote killing of tumor cells (5)



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PARIS

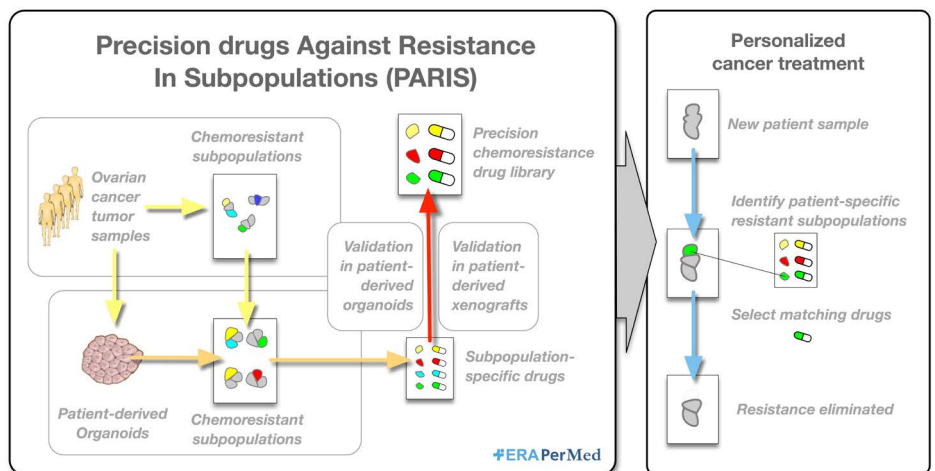
Precision drugs Against Resistance in Subpopulations

Chemotherapy resistance is the greatest contributor to cancer mortality, and the most urgent unmet challenge in oncology. Resistance is thought to emerge from small tumour cell subpopulations, and these resistant subpopulations are thought to differ between patients. This complexity makes the study and treatment of resistance extremely difficult.

The PARIS project (“Precision drugs Against Resistance in Subpopulations”) aims at the identification of the most common resistance subpopulations in ovarian cancer, and their treatment using drugs that target these subpopulations.

- To achieve its ambitious objectives, PARIS builds on, and develops:
- > a large collection of ovarian cancer samples
 - > leading-edge ovarian cancer models
 - > advanced single-cell measurement technology
 - > new high-performance algorithms to analyse the resulting large datasets
 - > leading-edge preclinical validation models
 - > extensive experience in the clinical management of ovarian cancer.


PARIS brings together laboratories in France, Finland, Denmark, and Norway that each specialise in one or more of these aspects. If successful, the project will result in a library of drugs that can be used to target the specific chemoresistance mechanisms active in each patient’s tumour cell subpopulation – a paradigm shift in personalised oncotherapy.





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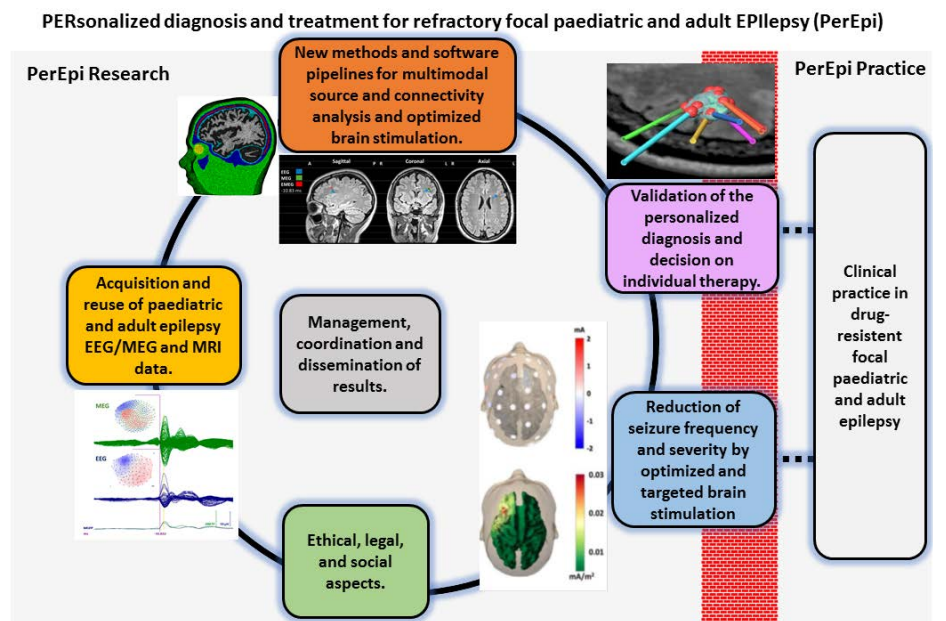
 Fabrice Wallois, Inserm U 1105, GRAMFC, Research Group on Multimodal Analysis of cerebral Function, France

PerEpi

Personalised diagnosis and treatment for refractory focal paediatric and adult epilepsy

Epilepsy is among the most frequently diagnosed pediatric and adult neurological disorders. Only in two-thirds of the patients, seizures can be adequately controlled with drug treatment. For the remaining drug-resistant patients with focal epilepsy, epilepsy surgery is currently the most effective treatment. However, only a fraction of those patients are eligible for epilepsy surgery. That is either because the epileptogenic zone in the brain cannot be localised with sufficient accuracy, or because it cannot be surgically removed without considerable neurological deficit.


PerEpi aims to improve this situation in two ways, both of which use concepts of non-invasive personalised medicine. The first one focuses on a new individualised multimodal approach to improve the localisation accuracy of the epileptogenic zone in order to offer the most appropriate personalised therapy. The second one focuses on a new individually optimised transcranial brain stimulation technique as a new treatment option to reduce seizure frequency and severity. This is particularly attractive for those patients with refractory focal epilepsies where surgery is not an option. A dedicated ethics work package will ensure that the research in the consortium is designed and conducted following the highest ethical standards and that responsible clinical integration is fostered.





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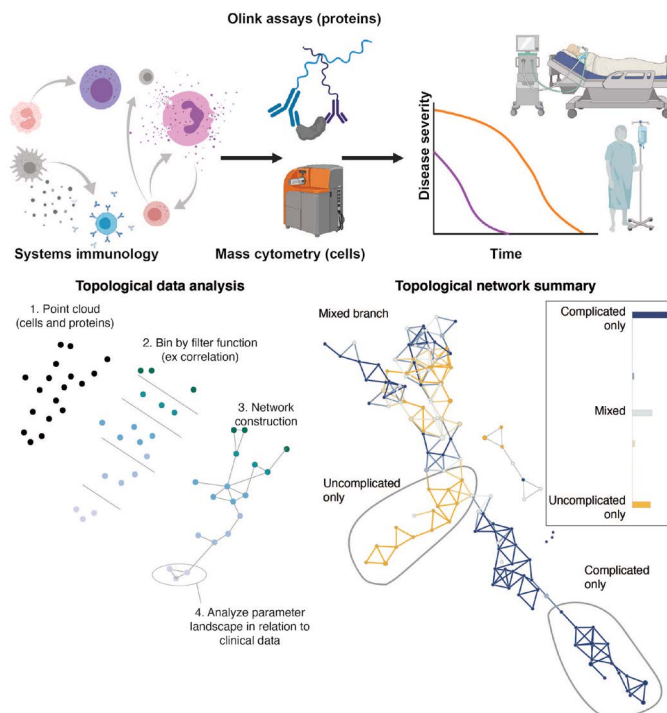
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PerMIDRIAR

Personalised medicine to tackle immune dysfunction in refractory juvenile idiopathic arthritis


Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory disease of joints in childhood. Despite novel therapeutic options, a number of children with JIA do not achieve an inactive disease, resulting in a lifelong burden. We will focus on these particularly sick children. In our well-established longitudinal cohorts of all participating countries (Canada, the Netherlands, Germany, Sweden, Italy) we have collected detailed data (information of patient history) and blood samples. From this data, we will identify the subgroup of high-risk children and perform an analysis on immune cells of the blood and arthritic joints using novel analytical methods (Fig. 1.) together with available patient data (Fig 2.) to identify mechanisms and origins of the disease. We will also integrate data on socio-economic background, including regional differences in access to medications, to see whether this affects therapeutic success (Fig. 3 and 4.). Using this approach we will identify and evaluate disease markers prospectively in new patients of our cohorts. Our consortium will thereby characterise key pathways – biological, clinical and societal, which predict therapeutic response and identify those patients with a particular risk for developing a severe disease. This is the first step towards a personalised medicine approach to tailor individualised strategies to improve outcome for affected children with JIA.





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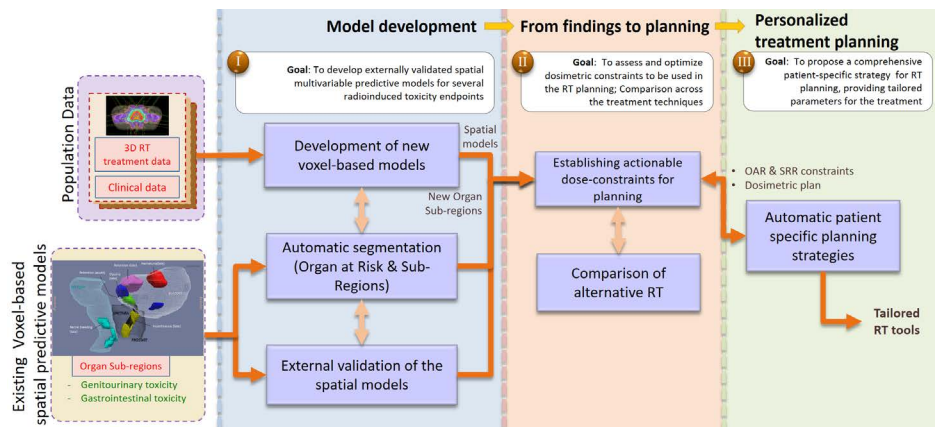
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PerPlanRT

Personalised Planning in RadioTherapy Through Integrative Modeling of Local Dose Effect and New Dosimetric Constraints


Radiotherapy (RT) for prostate cancer (PC) involves irradiation not only of the target volume but also of portions of healthy neighboring Organs at Risk (OaR) such as bladder, rectum or penile bulb. RT-induced morbidity of sexual, urinary, or rectal nature can arise, impacting Quality of life (QoL). RT protocols are currently optimised on the former assumptions that the radio-sensitivity and the functionality are uniform within the same OaR. Image mining of 3D dose distribution in low spatial scales, via voxel-based population methods, has highlighted the existence of radiosensitive sub-regions (SRR) responsible of radio-induced toxicity. Modern RT protocols have not yet incorporated these findings due to the lack of i) extensive validation ii) dosimetric constraints for plan optimisation and iii) automated patient-specific SRR contouring methods. The goal of PerPlanRT is to devise innovative decision-making tools aimed at proposing integrated and feasible strategies for personalised RT in PC with reduced RT-induced toxicities. Multivariable spatially accurate predictive models derived from large set of cohorts prospectively collected will be applied to different RT scenarios to explore their patient-specific benefits in depth. The application of these models to the clinical practice will be performed through the generation of dose distributions adapted to patient-specific anatomies.





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 Norbert Paul, University Medical Center, Johannes Gutenberg University, Germany

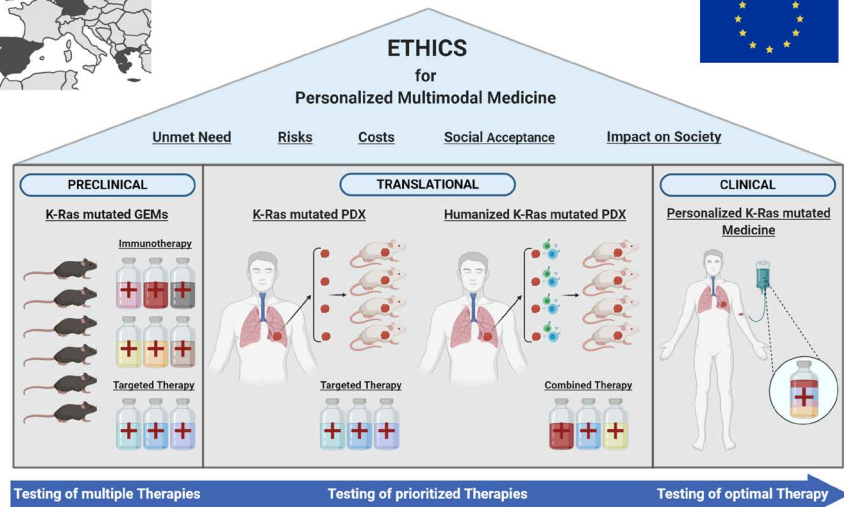
PMT-LC

Personalised multimodal therapies for the treatment of lung cancer

Lung cancer is the number one cancer-related killer worldwide and less than 20% of patients survive five years. Current treatments for lung cancer are initially effective, but acquisition of resistance almost inevitably occurs in most patients. The main aim of the consortium is, therefore, to develop effective personalised treatments that combine individual oncogenic targets with additional anti-cancer compounds and in particular with anti-cancer immune therapy. For optimal translation between basic research and clinical application, preclinical research will first validate the efficacy of novel personalised therapies in genetically engineered mice (GEMs) that recapitulate oncogenic lung cancer driver mutations found in patients. In parallel, we will select lung cancer patients that harbour identical driver mutations, evaluate their immunological baselines, take biopsy samples and use these for patient derived xenograft (PDX) therapy validation. Since the final aim of the consortium is to develop effective personalised treatment, we plan a first investigator initiated clinical trial (IICT) for testing the most beneficial therapy in pre-selected patients. Because personalised medicine raises novel ethical and socio-economic questions, one participating group will investigate how elevated treatment costs are socially justified and how normative concepts of individualised approaches in personalised cancer therapy can be best implemented.




ERA PerMed





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Preserve

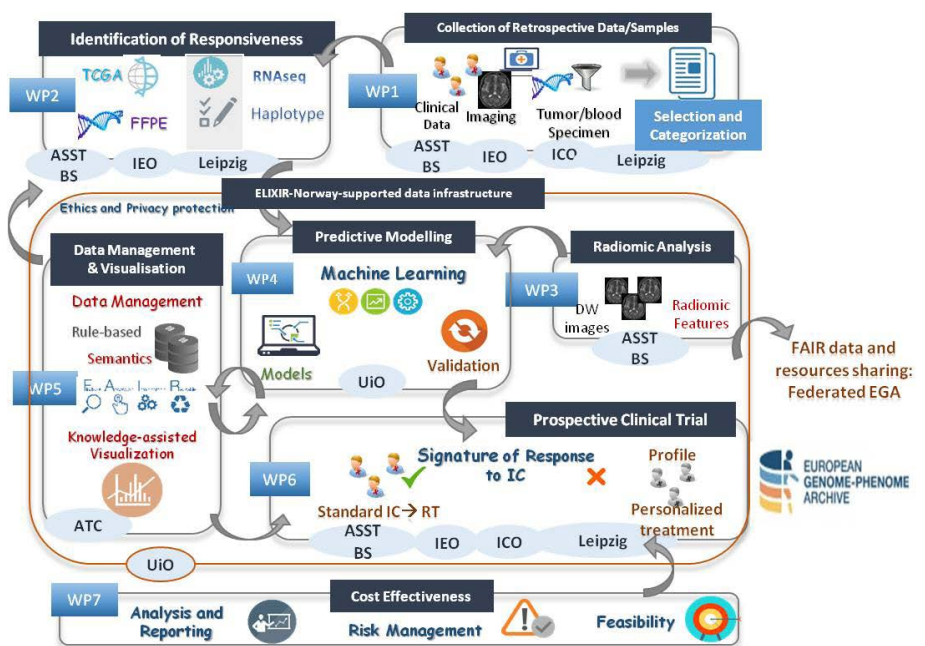
AI for new signatures and models for tailored organ preservation approaches in laryngeal and hypopharyngeal cancer

Locally advanced laryngeal (LAR) and hypopharyngeal (HYPO) squamous cell carcinoma may be treated with induction chemotherapy (IC) followed by radiotherapy (RT) for larynx preservation (LP) as an alternative to total laryngectomy (TL). However, not all patients benefit from LP strategy and up to 30-40% end up having a TL. The current proposal will personalise patients' management to increase the rate of LP, by maximising the probability of response to induction treatment.

Preserve will collect and integrate a large series of clinically annotated data from LAR/HYPO cancer patients treated with IC followed by RT, to assess a multi-omic signature of response to IC and to define alternative pathways. Transcriptomic analysis, molecular data on cell lines and radiomic evaluation will be main components of this signature.

Our predictive models integrated into an intuitive clinical decision support system will be validated in a phase II feasibility trial with tailored systemic induction treatments, according to the discovered signature, providing evidence for clinical translation.


A cost-utility analysis of our personalised treatment in LAR/HYPO cancer integrating quality of life measures will assess sustainability of personalised medicine in clinical setting.





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PROGRESS

PRecisi**O**n medicine in CAD patients: artificial intelli**G**ence for integ**R**ated g**E**nomic, functional and anatomical a**S**essment of the coronary collateral circulation

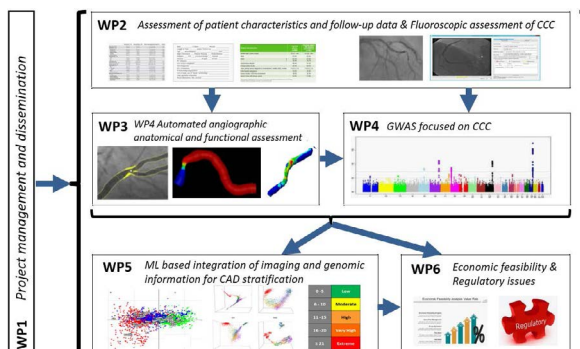
Coronary artery disease (CAD) is a major burden for patients and healthcare systems worldwide. The most common cause of CAD is atherosclerosis, an inflammatory disease on with life-threatening effects in the coronary circulation. Often, the circulation adapts through collateral artery formation, leading to significantly improved long-term post-ischemic outcome.

Hence, timely determination of the collateral profile presents a pivotal factor in the personalised treatment of CAD.

However, the coronary collateral circulation (CCC) development is not well predicted by traditional CAD risk factors. Moreover, manifold inconsistencies are still apparent in CCC research, mainly associated with the difficulty of quantifying CCC accurately and reproducibly. Therefore, the overarching objective of PROGRESS is to develop a tool for more accurate, reproducible and automated prediction of patients’ potential to develop CCC, which could be used for a more efficient CAD patient management.

We will harness Artificial Intelligence (AI)-based angiogram image and genetics analyses aiming to improve risk stratification and management of CAD patients, based on their CCC formation profile. This will be followed by timely application of therapeutic approaches in order to stimulate CCC formation and thus improve survival rates of patients after diagnosis.


We have collected well-powered CAD cohorts with genetic and imaging data. AI-based image analysis will aid in phenotyping CCC and also in generating post-hoc surrogate functional parameters (validated against a cohort of invasively phenotyped patients) in an unbiased fashion. This provides the basis for a genome-wide association study (GWAS) on CCC performed in large detection and validation cohorts.





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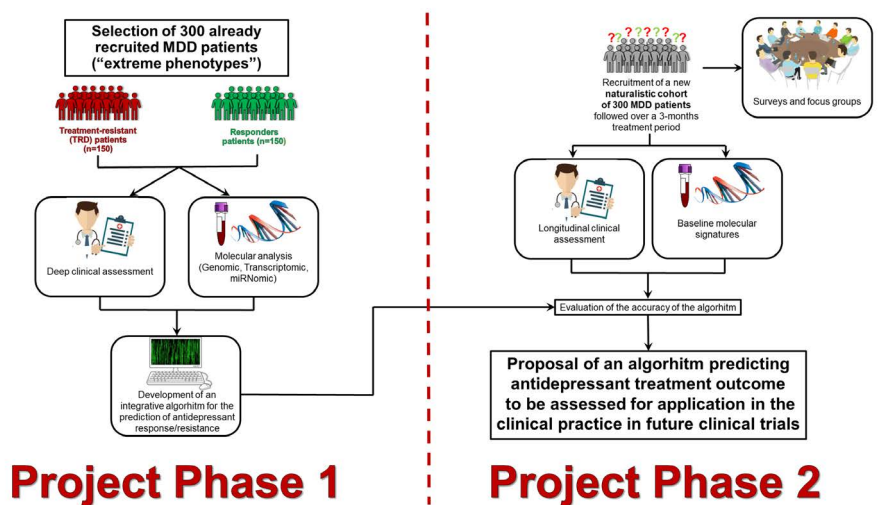
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PROMPT

Toward PRecisiOn Medicine for the Prediction of Treatment response in major depressive disorder through stratification of combined clinical and -omics signatures


Major depressive disorder (MDD) is the most common psychiatric disease worldwide, with huge socio-economic impacts. Pharmacotherapy represents the first-line therapeutic choice, but about 30% of patients are classified as resistant to treatment (TRD). TRD is associated with specific clinical and biological features; however, taken individually, these signatures have limited power in response prediction. The project's aim is the development of an innovative algorithm for the early detection of non-responder patients, more prone to later develop TRD. Phase 1 will involve 300 patients with MDD already recruited, including 150 TRD/150 responders, considered as "extremes" in relation to treatment response. A full clinical assessment will be performed, together with a comprehensive molecular evaluation (genomic, transcriptomic and miRNomic profiling). An algorithm integrating all these data will be developed in order to predict response to therapy. In phase 2, a new cohort of 300 MDD patients will be recruited to assess, in real-world conditions, the ability of the algorithm to correctly predict treatment outcome. Moreover, an active participation of patients will be established to consider their perspectives and needs. Project results will provide a new predictive tool for future use in the clinical practice, enabling a better prevention and management of MDD treatment resistance.





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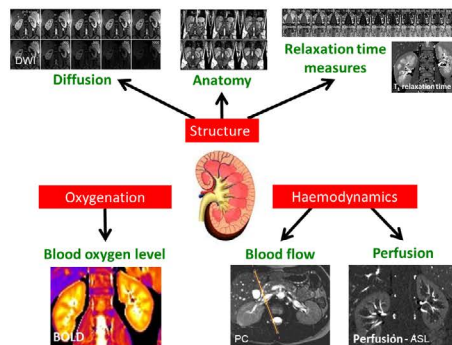
 Susan Francis, University of Nottingham, UK

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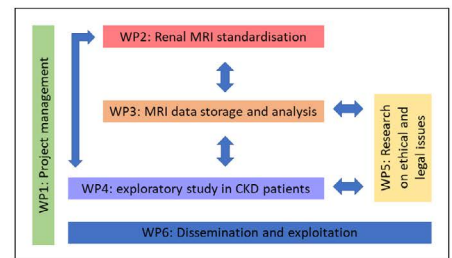
RESPECT

Renal MRI standardisation to improve personalised management of CKD patients

Chronic Kidney Disease (CKD) represents a global and increasing health burden with high economic cost. CKD patients exhibit a progressive disease, nonetheless a failure of current therapies has been demonstrated and an alarming number of clinical trials have failed. Better methods are urgently needed for earlier diagnosis and improved patient stratification, targeted treatment, and monitoring. Renal multiparametric Magnetic Resonance Imaging (MRI) has emerged as a promising non-invasive technique for characterisation of renal physiology and pathophysiology. However, current methodological differences across studies hinder reliable comparisons, and additional evidence for clinical validity and utility of renal MRI is required. RESPECT addresses these unmet needs with a multinational, multidisciplinary and intersectoral project that will set up and technically validate a scalable standardised renal MRI infrastructure, allowing multicentre clinical research. The project will also set up an open-access platform for renal MRI data sharing and processing, taking advantage of latest artificial intelligence developments, and will develop MRI data sharing guidelines taking patient, healthcare and ethic professionals’ perspective into account. The project will finally provide preliminary cross-institutional evidence of renal MRI feasibility and utility in characterising and staging CKD. This is fundamental for renal MRI ultimate transfer to clinical practice for personalised medicine.




Renal MRI standardization to improve personalised management of CKD patients (RESPECT)





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TIPS

Tailored Immunotherapy for Paediatric SIRS

TIPS is a project on personalised medicine for improved understanding and management of paediatric severe inflammatory response syndrome (SIRS). SIRS, which can affect children without predisposing factors is a life-threatening event due to an uncontrolled activation of the immune system as a results of, often, unknown triggers. For the majority of patients, acute management of SIRS is based on clinical features and routine laboratory parameters without distinct stratification, demonstrating the need for better and precise diagnostics. We aim to generate personalised immune profiling and to identify diagnostic patterns in order to develop individualized therapies to improve patient outcome. In this transnational endeavour, we will integrate consideration of ethico-legal aspects of patient safety and data protection.

Project TIPS is co-coordinated by S. Brenner and S. Thieme from the Department of Pediatrics, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany

