This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR PROJECTS – v1.1

For more information on the ESR projects, contact at call@improvepd.eu

ESR1	**Longitudinal PD risk profiling and CV outcome analysis (WP1)**	**UKL-HD**

Organisation official name

Universitaets-Klinikum Heidelberg

City	Country
Heidelberg	Germany

About the Institute/Group

The ESR will work within a cooperation of the Heidelberg Pediatric Nephrology Research Group together with the Institute of Medical Biometry and Informatics (IMBI). The group coordinates the Int. Pediatric Dialysis Network, the International Paediatric PD Biobank, the ESCAPE, 4C, PodoNet and EURenOmics Consortiums. The IMBI is involved in data management and statistical analysis. Via Improve-PD the group has access to further large int. PD databanks.

Description of the ESR project

Objectives:

The ESR will combine key peritoneal dialysis (PD) databank and bio-repositories, to create an intersectoral data platform across age groups and including details on PD treatment modalities, pharmacotherapy, time-integrated biochemical profiles, social factors and health care systems. The combined data sets will be used to evaluate therapy-related factors influencing cardiovascular risk in PD patients. This will include established factors, (details of the PD prescription and clearance efficacy, fluid overload, infectious and non-infectious complications, and comorbidity), and aspects of PD treatment that have not been adequately evaluated such as gender, pharmacotherapy and parameters of cardiovascular health documented in subsets of patients biochemically, by imaging and blood pressure monitoring. Findings will be compared with the hemodialysis population, using the data available to this consortium from patients followed in pediatric and adult registries and clinical trials.

Expected Results: The ESR will develop a risk factor panel and algorithms allowing PD adequacy estimation and identification of patients which should benefit from novel PD fluids / innovative PD regimens. Analysis of factors predictive of adverse outcome in PD versus HD patients will serve as basis to help deciding which patients should undergo a modality switch in clinical practice.

Candidate description

This unique opportunity requires an enthusiastic candidate, willing to interact and cooperate across scientific and geographic borders with different international research centers for combining the data and subsequent detailed statistical analyses. The position presupposes a strong background in (bio) statistics, mathematics, data science or a related field. Willingness to understand the clinical background is a must. Furthermore, sound oral and written communication skills in English are necessary.

Required skills (500 characters including spaces and no more than 5 bullet points)

- In-depth knowledge of key biostatistics, including analysis of longitudinal and multivariate data and handling of missing values
- Very good programming skills in statistical software such as R or SAS
- Strong motivation and ability to collaborate in an interdisciplinary team
- Analytical and structured way of working and a high degree of quality awareness and sense of responsibility
- Excellent communication skills in English (and preferably also in German)

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ESR2	The peritoneal and vascular histology, transcriptome and proteome in uraemia and PD (WP1)	UKL-HD

Organisation official name

Universitaets-Klinikum Heidelberg

City	Country
Heidelberg	Germany

About the Institute/Group

The Pediatric Nephrology group and cooperating partners offer all state of the art research and training facilities, a unique training is provided. The group coordinates the Int. Pediatric Dialysis Network, the Int. Pediatric PD Biobank, and the ESCAPE, 4C, PodoNet and EURenOmics consortia. The central bio repository holds 44000 aliquots from 3000 children with renal diseases and 600 peritoneal specimens. Access to respective adult biobanks is available in Heidelberg and in cooperating centres.

Description of the ESR project

Objectives: The ESR will histomorphometrically describe peritoneal and arterial specimens from healthy, uremic and PD treated children and adults from Heidelberg, Cardiff, and Madrid biobanks. Findings will be related to PD treatment modalities, clinical disease spectrum and inflammatory complications. Molecular mechanisms will be assessed by whole exome profiling, and (in secondments) by proteomics, miRNA sequencing, and (omental) metabolomics. Key findings will be validated in independent cohorts, compared with findings in HD patients and cross-validated in experimental settings. The human *ex vivo* findings will also serve for validation of experimental data obtained in other groups of the consortium and provide molecular patterns to interact with by development of novel PD fluids.

Expected Results: Molecular characterization/pathway identification of uraemia, and PD induced tissue damage and vascular disease. The project will provide a data warehouse which will allow for validation of present and future experimental PD studies in humans and define pathomechanisms, novel PD fluids should interfere with locally and with regard to systemic cardiovascular disease (CVD).

Candidate description

The ESR will be placed in a unique interdisciplinary network of PhD and postdoc fellows in Heidelberg and cooperating centres. She/he should be highly interested in histopathology and in-depth molecular tissue analyses and experimental PD research with close clinical background, and enthusiastically advance skills and knowledge to substantially contribute in the field of PD.

Required skills

- Proficient knowledge of respective key molecular biology methods and understanding of omics technology
- Previous medical training is not mandatory, but great interest in the field of dialysis is expected as well as passionate aspiration for advancing the scientific understanding of PD and associated CVD
- The project requires flexibility, interdisciplinary cooperation and mobility
- Proficiency in scientific English and experience in writing scientific manuscripts are appreciated

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR3	Inter-relationship of intraperitoneal inflammasome to systemic inflammatory response, hypoalbuminaemia and worsening cardiovascular and hydration status (WP1)	KU

Organisation official name

Keele University

City	Country
Keele	United Kingdom

About the Institute/Group

The Renal Research Group at Keele University is a world leader in PD research. Led by Prof. Simon Davies (President: International Society of Peritoneal Dialysis, 2010-12; EuroPD, 2017) the group includes Mark Lambie (Senior Lecturer) and Ivonne Solis-Trapala (Bio-statistician). It is located within the Faculty of Medicine and Health Sciences on the Keele University Campus with close connections to the University Hospital of North Midlands. The Faculty encompasses a Clinical Trials Unit and strong methodological research expertise including prognosis research (Prof Richard Riley), epidemiology (Prof Danielle van der Windt) and big data analysis (Prof Mamas Mamas).

Description of the ESR project

Objectives: The ESR will examine longitudinal interactions between cardiovascular comorbidity, outcomes, hypoalbuminaemia and peritoneal membrane transport status in GLOBAL, PD-CRAFT and UK-Shanghai bioimpedance trial cohorts, and compare with HD (ALCHEMIST Cohort and ongoing BISTRO Trial). Registry-based evaluation of relationships will be identified (UKRR, ANZDATA).

Expected Results: To establish the extent by which systemic inflammation is driven by longitudinal peritoneal inflammatory change, including that resulting from peritonitis episodes, in the context of the inflammatory genotype. Integration of these findings with cardiovascular and pro-fibrotic biomarkers (albumin, IL-6, CRP, NT-proBNP, PINP, PIIINP, ICTP, Galectin-3, ST-2, CT-1, NGAL, complement) to develop an enhanced prognostic model for high-risk phenotypes that can be used for improved risk stratification and provide rationale for future tailored interventions and personalized medicine.

Candidate description

You will either be a methodologist interested in specialising in the use of data to understand illness (e.g. epidemiology, prognosis and disease progression) or a medically qualified doctor who wishes to have an academic career, particularly in the field of kidney disease and dialysis medicine, working with clinical data.

Required skills

- Experience in handling data (such as the use of electronic databases and statistical support packages, e.g. ML-WIN, R) is very desirable but not absolutely essential, provided you are comfortable working with mathematical approaches.
- You will be well supported in gaining or advancing your statistical skills, but evidence of prior training will be considered favourably in your application (e.g. Masters modules in biostatistics, postgraduate training).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR4	Developing a pro-fibrotic cardiovascular disease fingerprint associated with CV outcomes in PD (WP1)	INSERM

Organisation official name

Centre d'Investigation Clinique Plurithématique Pierre Drouin 1433 –INSERM- CHRU de Nancy-Université de Lorraine

City	Country
Nancy	France

About the Institute/Group

With its staff specifically dedicated to clinical research, CIC acts as an interface between basic research and completed medical research, and its purpose is to produce new scientific and medical knowledge in compliance with ethical and legal standards. Capacity and resources: Cohorts, Biobanking, Measurements of biomarkers, biostatistics, coordination of a national network of excellence (F-CRIN Cardiovascular and Renal Clinical Trialists (INI-CRCT, http://www.inicrct.org/en/home)

Description of the ESR project

The main research focus of our group is the interplay between cardiac, vascular and renal diseases, with a translational approach and a high level of scientific production. The team is currently coordinating international collaborative studies focusing on cardiac fibrosis biomarkers and impact of mineralocorticoid receptor antagonists (MRAs) on CV outcomes.

Objectives: The ESR will use the databases and biosamples available to the consortium (both clinical and preclinical) to assess the correlations between fibrosis and inflammation biomarkers, and the additional value of fibrosis biomarkers with respect to existing "classical" biomarkers (PINP, PIIINP, ICTP, Galectin-3, ST-2, CT-1, NGAL) and newer ones identified by other ESRs for better prediction of CV outcomes. Specificities of patients in PD (treatment modalities, underlying diseases) will be compared to those of patients in haemodialysis.

Expected Results: The definition of mechanistic biomarker phenotypes associated with specific CV outcomes may allow a "pharmacophenomics" approach for future biomarker guided treatment strategies and individually targeted pharmacological treatments that could lay the ground for successful CV prevention and treatment strategies in CKD patients on PD.

Candidate description

She/he may have either a more epidemiological or biological background but the objective of this PhD project is to develop an integrative approach and she/he will have to develop the skills that may be lacking at baseline. Self-learning may be required but the dynamic team will help her/him to develop her/his knowledge. The CIC offers a diversified research environment to reliable and highly motivated students! Master degree of epidemiology or (bio)statistics or clinical research is required.

Required skills

- Medical background in nephrology or cardiology OR biological background
- Capacity to perform basic statistical analyses (descriptive statistics, basic survival analyses)
- Capacity to interact with the statistical team of the group for more complex statistical analyses if necessary – ability to drat a statistical analysis plan
- Proficiency in English or French
- Experience in writing scientific manuscripts appreciated

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR5	Evaluation of mesothelial to mesenchymal transition (MMT)-biomarkers in peritoneal dialysis (PD) and in cardiovascular disease (CVD) (WP1)	CSIC

Organisation official name

Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC)

City	Country
Madrid	Spain

About the Institute/Group

The group of Dr. López Cabrera is located at the Centro de Biologia Molecular Severo Ochoa (CBMSO), a mixed Center composed by researchers from CSIC and Universidad Autonoma de Madrid. This group leads a multidisciplinary team with internationally recognized expertise in basic and clinical aspects of peritoneal dialysis (PD). This Group was the first in the identification of the mesothelial to mesenchymal transition (MMT) process in PD patients and demonstrated that MMT is a key and targetable mechanism for peritoneal damage. The group has attracted research funding, at national and international levels, from both public and private sectors. CBMSO has excellent infrastructure and facilities necessary to offer a suitable environment for training and experimental research.

Description of the ESR project

Objectives: This Group has identified a number of biomarkers that may have diagnostic/prognostic value for peritoneal membrane deterioration and cardiovascular outcome in PD patients. The ESR will study MMT-associated markers in PD effluents and in plasma from chronic kidney disease (CKD), peritoneal dialysis (PD) and haemodialysis (HD) patients and correlate these with peritoneal membrane function, cardiovascular disease and patient outcome. The role of candidate markers linking MMT, vascular EndMT (endothelial to mesenchymal transition) and CV disease will be analysed in human samples and in animal models with regard to local and systemic fibrotic and inflammatory effects and cardiovascular sequelae.

Expected Results: Validation of an MMT biomarker chip for prediction of morphological and functional peritoneal membrane transformation and with regard to CVD. Molecular mechanisms linking peritoneal and CV disease will be described and findings translated into the development of novel PD fluids.

Candidate description

Outstanding graduates in the fields of biomedical sciences, medicine or biochemistry are invited for application. An ideal candidate will have a solid interest in clinical research and knowledge of data analysis. The position requires solid analytical thinking and prior lab experience will be considered. Knowledge in omics technologies and in statistical methods will be of advantage.

Required skills

- Background in medicine or life sciences (MSc or equivalent that qualifies to enrol for a PhD program at the Universidad Autónoma de Madrid)
- Good skills in English (written and spoken)
- Skills in data science, including motivation to expand statistical and bioinformatics
- Certification to handle experimental animal models will be of advantage
- Skills for lab techniques, willingness to work with human samples and animals

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR6	Humoral factors communicating peritoneal to systemic inflammation and cardiovascular disease (WP2)	UAM

Organisation official name

Universidad Autónoma de Madrid. Faculty of Medicine
Department of Medicine at the Fundación Jimenez Diaz
Molecular and Cellular Biology in Renal and Vascular Pathology

City	Country
Madrid	Spain

About the Institute/Group

Our group is investigating the molecular mechanisms involved in chronic renal diseases and related cardiovascular pathologies (to remark; Circ Res. 2000;86:1266-72; Circulation 2005;111:2509-17) to improve patient treatment. Some important findings include novel mediators, such as Connective tissue growth factor (Circulation 2003;108:1499-09; J Pathol. 2018;244:227-41) or Gremlin (Clin Sci 2018;132:1097-15), and epigenetic targets (J Am Soc Nephrol. 2017;28:504-19).

Description of the ESR project

Objectives: The ESR will evaluate mechanisms of peritoneal to systemic inflammatory communication. Using contemporary techniques (mRNAseq, microRNAseq, proteomic) the ESR will profile local and systemic inflammatory change, and will study their reciprocal control and communication to the vasculature. The ESR will use the established nephrectomy-PD infusion model in ApoE knockout animals, available *in vitro* cellular models, and (v*ia* secondment) established models of infection-associated peritoneal inflammation.

Expected Results: Identification of the key components of peritoneal-cardiovascular cross-talk between inflammatory response and progression of atherosclerosis in an established atheroma-prone mouse line. These studies will provide a needed understanding of the inter-relationship of peritoneal and systemic inflammation, promoting understanding of recent and planned (WP1) studies in material from patients, and a framework for studies of targeted anti-inflammatory intervention (WP2).

Candidate description

A PhD student (Master required) of Biomedical Sciences (Biochemistry, Molecular Biology or similar) with previous experience in biomedical research. The student will be involved in experimental design, data interpretation and analysis of the findings. The experiments will include mice handling and surgeries, cell culture experiments and many laboratory techniques (classical and omics). The ability to communicate findings to diverse audience and to collaborate with other researchers will be essential.

Required skills

- Training course in Laboratory Animal Science for scientists.
- Master required.
- Some skills will be positive evaluated: Different laboratory techniques (cell culture, protein isolation, PCRs, flow cytometer, others), histology and pathology related tools (confocal microscopy). Use data bases and bioinformatics tools.
- Previous experience in mRNAseq, microRNAseq, proteomic will be taking into account.
- Other skills: communication, problem solving, and positive social interaction.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR7	The role of the peritoneal barrier in controlling the local-systemic inflammatory link (WP2)	UCL

Organisation official name

Pole of Nephrology, Institute of Experimental & Clinical Research, UCLouvain, Brussels

City	Country
Brussels	Belgium

About the Institute/Group (limit 500 characters including spaces)

The UCLouvain group is using cellular and animal models, human cohorts and databases to investigate the molecular mechanisms of transport and inflammation in the peritoneal membrane, taken as a model tissue for structural changes. Recent studies include: Morelle et al. *JASN* 29: 1875-86, 2018; Festa et al. *Nat Commun* 9: 161, 2018; Corre et al. *JASN* 29: 335-48, 2018; Hautem et al. *JASN* 28: 2038-52, 2017; Pattaro et al. *Nat Commun* 7 : 10023, 2016 ; Morelle et al. *JASN* 26: 2521-33, 2015; Tyteca et al. *PLoS One* 10 : e0117398, 2015 ; Yool et al. *JASN 24*: 1045-52, 2013; Trudu et al. *Nat Med* 19: 1655-60, 2013.

Description of the ESR project

Objectives: The ESR will determine how changes in peritoneal barrier function as a consequence of peritoneal dialysis (PD) alter peritoneal/systemic immune crosstalk, and the resultant effects on systemic cardiovascular phenotype. A focus is the role of the water channel aquaporin-1 (AQP1) in vascular proliferation and fibrogenesis in the peritoneal membrane. The ESR will characterize the relationship between structural changes in the peritoneal membrane (vascular changes, fibrosis, infiltrate) and modifications in the transport of small solute and water and identify and characterize pharmacologic agents regulating the expression or activity of AQP1. The ESR will use well-established mouse models of exposure, transgenic lines (*Aqp1*, *Aqp7*, …), cellular models, and correlations with genetic and functional data and analyses on peritoneal biopsies.

Expected Results: Defective water transport and fluid overload are major drivers for cardiovascular complications in PD. The present studies will extend our knowledge of the role of peritoneal barrier function in controlling peritoneal-systemic immune crosstalk, and on water channels in physiologic and pathologic conditions.

Candidate description

Candidates must hold a MSc degree in biology, medicine, biomedical sciences, pharmacy, or veterinary medicine. Knowledge of English is required. Willingness to work on in vitro and in vivo systems. An 'international mobility' status is required for this position (i.e. not having resided or worked in Belgium for more than 12 months in the 3 years before the recruitment date).

Required skills

- Interest for innate immunity, fibrosis, angiogenesis and inflammation
- Interest to learn molecular and cell biology techniques
- Willingness to work on mouse models and cellular lines
- Interest for translational studies extending to patients on dialysis
- Team spirit and collegiality

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR8	Mechanisms of cardiovascular damage following bacterial peritonitis (WP2)	CU

Organisation official name

Cardiff University

City	Country
Cardiff	United Kingdom

About the Institute/Group

Peritoneal dialysis and immunity is a longstanding and major research theme in Cardiff University. The work takes place in Wales Kidney Research Unit, a nationally-funded biomedical research unit in which there is close working between scientists, clinicians, and patients. The main supervisor, Dr Anne-Catherine Raby (http://www.cardiff.ac.uk/people/view/126661-raby-anne-catherine) has worked extensively in innate immune responses in the peritoneum, and this work is published in leading kidney journals including Journal of The American Society of Nephrology and Kidney International, and in general journals including Journal of Biological Chemistry and Science Translational Medicine.

Description of the ESR project

Objectives: The ESR will use an *in vivo* model of peritoneal infection (developed in our laboratory) for which there is a well-defined local inflammatory response in order to study the systemic sequelae of the infectious episode(s). The ESR will evaluate vascular and cardiac changes in wild type and susceptible (ApoE --) animal models, employing different strains of bacteria clinically relevant in this context. *In vitro* experiments will also be conducted to identify the immune receptors involved in these changes.

Expected Results: 1. Determine systemic immune responses to acute bacterial peritonitis; 2. Investigate the cardiovascular changes induced by a single or repeated bacterial peritonitis episodes; 3. Mechanistic understanding of observed systemic alterations/pathology

Candidate description

We are seeking to appoint a highly motivated candidate to undertake PhD-level training in the area of infection and immunity, applied to cardiovascular disease in peritoneal dialysis patients

Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or an equivalent qualification gained outside the UK in Biomedical or Immunology-related degree. A Master's degree (or equivalent) and/or additional significant relevant laboratory experience are desirable.

We encourage interested applicants to contact the program for informal discussion about the project and our laboratory environment.

Required skills

- Basic laboratory skills: use of pipettes. balances, volumetric glassware.
- Good knowledge of written and spoken English (equivalent to an ILETS ≥ 6.5 or evidence of a previous degree in English)
- Basic computer skills (Word processing, presentations, spreadsheets)
- Full training in the required lab methods will be provided, but prior knowledge of one or several of the following techniques is desirable: ELISA, western blot, tissue culture, DNA/RNA extraction, PCR.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR9	Hyaluronan (HA)-regulation of vascular smooth muscle cell phenotype in peritoneal dialysis (WP2)	CU

Organisation official name

Cardiff University

City	Country
Cardiff	United Kingdom

About the Institute/Group

Peritoneal dialysis and immunity is a longstanding and major research theme in Cardiff University. The work takes place in Wales Kidney Research Unit, a nationally-funded biomedical research unit in which there is close working between scientists, clinicians, and patients. The main supervisor, Dr Soma Meran is a clinical academic and senior lecturer who has recently completed a four-year MRC Clinician Scientist Fellowship. Her research focuses on matrix-dependent regulation of cell phenotype relevant to progressive renal disease and cardiorenal disease.

Description of the ESR project

Objectives: The ESR will study extracellular matrix composition and organisation in the tunica media, to understand determinants of Vascular Smooth Muscle Cell Phenotype and resultant matrix calcification and arterial stiffness. State of the art matrix biology techniques developed in this and collaborating laboratories will be used, focussing on the expression and organisation of Hyaluronic Acid (HA). Mouse models established in the consortium (infection: CU, nephrectomy-PD: CSIC) will be used.

Expected Results: Characterise alterations in tissue expression of HA and HA-binding proteins in mouse models of (i) repeated peritoneal infection (ii) Uremia-PD infusion. Determine HA-dependent pathways causally linked to VSMC transdifferentiation. Confirm/refute involvement of candidate circulating factors identified by ESR 6 on medial matrix organisation and VSMC phenotype.

Candidate description

We are seeking to appoint a highly motivated candidate to undertake PhD-level training in the area of infection and immunity, applied to cardiovascular disease in peritoneal dialysis patients

Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or an equivalent qualification gained outside the UK in Biomedical or Immunology-related degree. A Master's degree (or equivalent) and/or additional significant relevant laboratory experience are desirable.

We encourage interested applicants to contact the program for informal discussion about the project and our laboratory environment.

Required skills

- Basic laboratory skills: use of pipettes. balances, volumetric glassware.
- Good knowledge of written and spoken English (equivalent to an ILETS ≥ 6.5 or evidence of a previous degree in English)
- Basic computer skills (Word processing, presentations, spreadsheets)
- Full training in the required lab methods will be provided, but prior knowledge of one or several of the following techniques is desirable: ELISA, western blot, tissue culture, DNA/RNA extraction, PCR.

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ESR10	Impact of local inflammation of progression of vascular calcification and uremic cardiomyopathy (WP2)	Amsterdam UMC

Organisation official name

Amsterdam University Medical Centre (Nephrology)

City	Country
Amsterdam	The Netherlands

About the Institute/Group

The Amsterdam Cardiovascular Sciences (ACS) institute is the research school of the Amsterdam University Medical Centre. It incorporates many state-of-the-art facilities for studying cardiovascular diseases in animal model, 2D and 3D cell models and ex vivo function testing, related to cardiovascular disease, with emphasis on (micro)vascular dysfunction and inflammation. The institute has a long track record of performing cutting edge science, and educating young researchers. ESRs will work within an international team of PhD students, technicians, and senior basic and clinical scientists.

Description of the ESR project

Objectives: To study the role of PD on the progression of vascular inflammation, atherosclerosis and calcification in several CKD rat model. In addition, myocardial function, perfusion and structure will be studied. To relate local peritoneal and systemic inflammation to uremic cardiomyopathy. Markers for inflammation will be tested, also incorporating progression of histological scoring of inflammation and calcification as a readout. Myocardial fibrosis, cellular infiltration and cardiomyocyte properties including contraction strength and calcium fluxes will be assessed. The impact of targeting identified specific components of inflammatory pathways will be modulated using siRNA.

Expected Results: PD-triggered inflammation determines both progression of vascular calcification and uremic cardiomyopathy. These typical pathological cardiovascular features of CKD can be attenuated by specific components of inflammation.

Candidate description

Based on the content of the ESR project, we are looking for a candidate (f/m) who is preferentially trained as a biomedical scientist, and skilled in analytical thinking and basic laboratory techniques. He/she is comfortable and productive working in a team, driven and curious, and speaks and writes fluently in English. The candidate has affinity with clinical problems, and can integrate basic and clinical science.

Required skills

- Curiosity
- Analytical thinking
- Team work
- Basic laboratory techniques
- English communication (oral/writing)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR11	The Role of the Microbiome for Cardiovascular Risk and the Mode-of-Action of a Novel Dipeptide containing PD Fluid (WP3)	ZYTO

Organisation official name

Zytoprotec GmbH

City	Country
Vienna	Austria

About the Institute/Group

Zytoprotec aims to develop innovative PD fluids and closely collaborates with the Christian Doppler Laboratory of Molecular Stress Research in Peritoneal Dialysis, a public/private partnership with the Christian Doppler Research Association located at the Medical University of Vienna.

The team identifies and develops novel cytoprotective PD fluids and aims to characterize their molecular mechanisms of action as well as molecular signatures as surrogate markers of clinical outcome in PD.

Description of the ESR project

Objectives: Zytoprotec has developed a novel PD fluid (PD-protec®), containing the dipeptide L-Alanyl-L-Glutamine (Ala-Gln) as cytoprotective additive. Based on preclinical data and promising results regarding modulation of stress responses and inflammation from two phase I/II trials, a best-in-class phase II study has been successfully completed for the novel PD fluid. The ESR will use the existing repository of clinical patient samples to delineate the impact of glutamine addition to PD fluid on the microbiome of PD patients. To this end, the ESR will perform animal experiments and connect molecular fingerprints (microbiome and metabolome) and phenotypic changes in CV outcome with PD patient data. Due to its close anatomical proximity the gut-peritoneum axis has the potential to explain the systemic anti-inflammatory effects of Ala-Gln. The ESR will have the chance to obtain validation samples from the phase III trial PD-protec®, where improvement of CV outcome might be an important clinical objective.

Expected Results: Microbiome and metabolomic profiles of PD fluid exposure and Ala-Gln addition in vivo. Effect of the microbiome in PD on CV outcome and vice-versa. Effect of fluid with added Ala-Gln (PD-protec) in a clinical phase III trial.

Candidate description

We invite applications from outstanding graduates in the fields of biochemistry, molecular biology, biotechnology and medicine. The ideal candidate will have a strong interest in clinical disease models and microbiome research. The position requires solid analytical thinking and prior lab experience is of benefit. Knowledge in omics technologies (including next generation sequencing (microbiome) and/or mass spectrometric analyses (metabolomics)) and interest microbiology and statistical methods will be of advantage.

Required skills

- Background in medicine or life sciences (MSc or equivalent that qualifies to enrol for a PhD program at the Medical University of Vienna)
- Excellent skills in written and spoken English
- High motivation, flexibility as well as innovate and creative thinking are a must
- Willingness to work with human samples and animals, including wet lab techniques
- Talent in data science, including a good basis of statistical and bioinformatic skills

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR12	From Mechanism to First-in-Human Application - Cardiovascular Effects of a Novel Kinase-Inhibitor-containing Cytoprotective PD Fluid (WP3)	ZYTO

Organisation official name

Zytoprotec GmbH

City	Country
Vienna	Austria

About the Institute/Group

Zytoprotec aims to develop innovative PD fluids and closely collaborates with the Christian Doppler Laboratory of Molecular Stress Research in Peritoneal Dialysis, a public/private partnership with the Christian Doppler Research Association located at the Medical University of Vienna.

The team identifies and develops novel cytoprotective PD fluids and aims to characterize their molecular mechanisms of action as well as molecular signatures as surrogate markers of clinical outcome in PD.

Description of the ESR project

Objectives: In search for novel cytoprotective additives, the class of glycogen synthase kinase 3 beta (GSK-3β) inhibitors was discovered. Thereof, lithium chloride was shown to be able to protect peritoneal cells from PD fluid induced cellular damage. The ESR will perform preclinical testing and conduct in vitro and in vivo experiments to analyse cardiovascular effects of this novel PD fluid.

The ESR will combine targeted molecular mechanistic analyses (morphology, markers of cell stress and survival, manipulation of gene expression) with systems biology techniques (omics) in order to characterize the molecular phenotype, generate hypotheses and test pathways involved in the mode of action.

Finally, the ESR will be involved in planning and design of a phase I/II trial (first-in-human application) to test safety and obtain preliminary efficacy data of the novel PD fluid.

Expected Results: Effects of kinase inhibitor supplemented PD fluid on endothelial cells (in vitro) and cardiovascular markers (in vivo). Molecular phenotype of PD fluid stress and mode-of-action of an icodextrin-based PD fluid with an added GSK-3β inhibitor. Clinical study synopsis for a first-in-human trial of a kinase inhibitor supplemented PD fluid, including surrogate markers deduced from in vitro and in vivo experiments.

Candidate description

We invite applications from outstanding graduates in the fields of biochemistry, molecular biology, biotechnology and medicine. The ideal candidate will have knowledge of standard and advanced molecular biology technologies (including cell culture, RT-PCR, siRNA, CRISPR/Cas, integration of omics data), experimental animal models and/or drug target research. The position requires solid analytical thinking and prior lab experience. A strong background in human biology and interest in statistical methods and translational medical research will be of advantage.

Required skills

- Background in medicine or life sciences (MSc or equivalent that qualifies to enrol for a PhD program at the Medical University of Vienna)
- Excellent skills in written and spoken English
- High motivation, flexibility as well as innovate and creative thinking
- Talent for wet lab techniques, willingness to work with human samples and animals
- Interest in data science, including motivation to expand statistical and bioinformatic skills

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR13	Preclinical study of a novel peritoneal dialysis fluid based on Stevioside as osmotic agent (WP3)	CSIC

Organisation official name

Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC)

City	Country
Madrid	Spain

About the Institute/Group

The group of Dr. López Cabrera is located at the Centro de Biologia Molecular Severo Ochoa (CBMSO), a mixed Center composed by researchers from CSIC and Universidad Autonoma de Madrid. This group leads a multidisciplinary team with internationally recognized expertise in basic and clinical aspects of peritoneal dialysis (PD). This Group was the first in the identification of the mesothelial to mesenchymal transition (MMT) process in PD patients and demonstrated that MMT is a key and targetable mechanism for peritoneal damage. The group has attracted research funding, at national and international levels, from both public and private sectors. CBMSO has excellent infrastructure and facilities necessary to offer a suitable environment for training and experimental research.

Description of the ESR project

Objectives: Glucose-based PD fluids induce inflammation and peritoneal membrane deterioration. Our group has developed, and patented, a novel biocompatible PD fluid in which Stevioside is used as the osmotic agent. Pre-clinical studies of Stevioside-based PD fluid showed an improved profile of peritoneal solute and water transport, and partial prevention of peritoneal membrane changes in mouse PD models. In understanding the mode of action of Stevioside, the ESR will focus on newly identified MMT- and vascular-related biomarkers to assess the inflammation/fibrosis/cardiovascular axis. The ESR will use biomaterial from preclinical testing to evaluate molecular effects of this novel osmotic agent in the peritoneal membrane and vessels, focussing on inflammation and CV parameters.
Expected Results: Mode-of-Action of a PD fluid based on Stevioside. Planning and design of a phase I/II trial to obtain safety and preliminary efficacy data of this novel PD fluid.

Candidate description

Outstanding graduates in the fields of biochemistry, molecular biology or biomedical sciences are invited for application. An ideal candidate will have a solid interest in clinical research and knowledge of standard and advanced molecular biology technologies, and experimental animal models. The position requires solid analytical thinking and prior lab experience will be considered. Knowledge in mouse models of disease, in omics technologies and in statistical methods will be of advantage.

Required skills

- Background in life sciences or medicine (MSc or equivalent that qualifies to enrol for a PhD program at the Universidad Autónoma de Madrid)
- Good skills in English (written and spoken)
- Certification to handle experimental animal models
- Skills for lab techniques, willingness to work with human samples and animals
- Interest in data science, including motivation to expand statistical and bioinformatic skills

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR14	Translation of research into development of a commercial PD fluid (WP3)	BAXTER

Organisation official name

Baxter Healthcare

City	Country
Vienna	Austria

About the Institute/Group

Baxter was the first producer of commercial PD fluids. There is core scientific knowledge and expertise related to epidemiology, statistics, health economics and strategic health planning. Baxter is supporting numerous research activities worldwide either through sponsored studies or investigator initiated research programs (Clinical Evidence Council).
PhD enrolment will take place at the Medical University of Vienna, a partner organisation of the IMPROVE-PD project.

Description of the ESR project

Objectives: This project focuses on the translation of pre-clinical and clinical findings into development of a commercial PD fluid in a typical private sector research approach. The ESR will apply latest state of the art technologies to tackle the problem that clinical development of novel PD fluids is virtually nonexistent, largely due to recruitment difficulties for adequately powered trials. He/she will (A) use data from existing cohorts to simulate PD trials in computer models to assess effects of introducing composite outcomes (indices) covering relevant major adverse peritoneal events, (B) explore preferences of PD patients PD by using qualitative methods to develop patient reported outcomes and outcome measures allowing optimized translation of commercial PD fluid development into clinical reality, (C) gain expertise in trial design/performance by working with Baxter Clinical/Medical Affairs to summarize patient outcomes and (D) gain expertise in innovative regulatory approaches (orphans designation, breakthrough pathways) for file submission to respective regulatory authorities – all tasks in close interaction with a cross functional team in an industrial environment.
Expected Results: Data on trial sizes, necessary to measure clinical outcome; Quantitative and qualitative description of PD patient preferences; Clinical development strategy for a commercial PD fluid

Candidate description

Outstanding graduates with a degree in medicine ("physician researcher") or life/health sciences and solid background in mathematics and statistics, or a degree in statistics/data science with a focus on medical application, are invited to apply. The ideal candidate will have a strong interest in translational and/or clinical research and biostatistics as well as mixed and qualitative research methods. The position requires solid analytical thinking and very good programming skills in statistical software such as R or SAS; prior experience in statistical methods and in qualitative research will be of advantage.

Required skills

- Background in medicine, statistics, mathematics, data science or life/health sciences (MSc or equivalent that qualifies to enrol for a PhD program at the Medical University of Vienna)
- Excellent skills in written and spoken German and English
- High motivation, flexibility as well as innovate and creative thinking
- Willingness to work at the interface of industrial and clinical research and collaborate across interdisciplinary and geographic borders
- Interest in translational research spanning from computer simulation to bedside

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 812699

ESR15	Using big data from the public domain for in-silico screening compounds with therapeutic potential in PD (WP3)	E3

Organisation official name

Epsilon 3

City	Country
Vienna	Austria

About the Institute/Group

Epsilon 3 is a bioinformatics start-up company focusing on digital drug development, and specifically finding alternative applications for existing drugs (repurposing). The main research direction is to identify substances interfering with pathomechanisms by overlapping drug and disease mode of action models derived from big data. Using this information Epsilon 3 offers solutions for drug repurposing of existing drugs, indication space screening for novel chemical entities and asset development in specific therapeutic areas, such as kidney failure.
PhD enrolment will take place at the Medical University of Vienna, a partner organisation of the IMPROVE-PD project, or alternatively at one of the other universities in Vienna.

Description of the ESR project

Objectives: The goal of this project will be to apply an *in-silico* platform for generating novel candidates of additives or drugs with the potential to counteract the inflammatory phenotype and lower CV risk in PD patients. This project will also integrate relevant pathomechanisms identified and forwarded from WP1 and WP2. The ESR will explore non-obvious mechanistic links in the big data platform utilizing information on protein coding genes and exploiting public domain data on multiple levels (text mining, omics data, protein interaction). The ESR will analyse and integrate large-scale data to build and understand molecular models and interference between them. In close collaboration with the ESRs in WP1 and WP2, ESR15 will generate entry points for precision medicine approaches and in-vivo testing of novel compounds.
Expected Results: Molecular models for PD- and CV-related pathomechanisms and candidate substances. Interference analysis of gathered molecular models. Shortlist of additional candidate compounds and drugs including mode-of-action data on compounds tested in WP 1-3.

Candidate description

The candidate holds a degree in computational biology, informatics, statistics or mathematics (Bachelor or Master degree) or has excellent knowledge in bioinformatics in combination with a life sciences or medical degree. Expertise in programming languages such as R, Python or Java as well as solid basics in molecular biology, data visualization and statistics are required. The strengths of the candidate include an efficient work style and networked thinking, accuracy and reliability. We are looking for an applicant with a strong interest in data science, organizational talent and team player skills who would like to contribute significantly to our research work and take part proactively in our scientific discussions.

Required skills

- Solid basics in computational biology (specific degree preferred)
- Excellent written and oral communication skills in English
- Highly motivated and well-organized working style
- Programming skills (R required, other languages and programs and concepts are a plus)
- Strong interest in data science and big data, network biology and statistics