ERA Operative Headquarters
Strada dei Mercati 16/A
43126 Parma, Italy
Tel: +39 0521 989078
fellowships@era-online.org
www.era-online.org

ERA Long-Term Research Fellowship Project

EuReCa-M

Project's key info

Title of the project	Sex differences in cardiovascular outcomes after kidney translaplantation
Working Group involved in the project	EuReCa-M
Principal Investigator(s) of the project	Liffert Vogt Amaryllis Van Craenenbroeck
Duration	12 months
Fellowship Grant	34.495,00 €
Start of the fellowship	Within 6 months after notification of the grant award to the fellow.

Receiving Institute

Name of receiving institute	KU Leuven
Supervisor's name	Amaryllis Van Craenenbroeck
Supervisor's e-mail address	amaryllis.vancraenenbroeck@kuleuven.be

Project's detailed description

Project description
This project investigates the impact of biological sex and donor–recipient sex mismatch on outcomes after kidney transplantation, with a particular focus on the role of endothelial cell biology. Sexual dimorphism in kidney disease is increasingly recognised, with documented differences in transporter expression, gene and protein levels, and glomerular cell biology. In kidney transplantation, these differences appear to translate into clinically relevant disparities. Although approximately 60% of kidney donors worldwide are female, around 60% of recipients are male. Survival outcomes differ markedly: female recipients experience higher excess mortality than males, while recipients of kidneys from female donors—particularly male recipients—have a higher risk of graft loss compared with those receiving grafts from male donors. Registry data suggest that grafts from female donors after brain death have up to a 1.5-fold higher risk of death-censored graft loss. Despite these observations, the underlying mechanisms remain poorly understood. The project hypothesises that, beyond hormonal influences, sex-specific differences in endothelial cell phenotype and function may drive these outcome disparities. Endothelial integrity, a key determinant of cardiovascular health and graft survival, remains underexplored in the context of donor sex and sex mismatch. The primary aims are to assess the effect of donor sex on all-cause mortality, cardiovascular mortality, and death-censored graft loss across different transplantation settings (donation after brain death, donation after circulatory death, and living donation), and to evaluate the impact of donor–recipient sex mismatch on the same outcomes. A further objective is to identify molecular pathways related to endothelial integrity that may explain the observed sex differences.

The study will use existing large-scale clinical datasets from the Dutch Organ Transplant Registry and the Leuven Kidney Transplant Cohort, with additional validation using national registries from the United States, Australia, and the United Kingdom. These clinical analyses will be complemented by transcriptomic, proteomic, and histological studies using kidney biopsy data and blood-derived samples, including single-nucleus RNA sequencing, bulk RNA sequencing, microarray data, spatial transcriptomics, and proteomic analyses.
By integrating epidemiological and multi-omics approaches, this project aims to provide mechanistic insight into sex-related disparities in kidney transplantation outcomes and to identify potential targets for improving graft survival and recipient health.

Goals of the project

The project aims at:

- Engaging the fellow in a high-impact research project
- Moving the field forward of cardiovascular disease after kidney transplantation
- Highlighting a potential crucial role of the endothelium in disease processes, both at the kidney level and systemic level (cardiovascular mortality)
- Contributing to impactful research
- Strengthening collaboration between experts in sex disparities, cardiovascular disease, and transplantation medicine

Qualifications and/or expertise required to the fellow

Qualifications of the candidate that are required for successful execution of the project are:
a background in clinical data science with specific skills in machine learning/advanced epidemiology/ modelling. Experience with cost-effectiveness analysis is desirable.