

The University of Extremadura in Badajoz, Spain, would like to propose a research internship opportunity to second year PhD students at participating EU Green Universities to boost international mobility and leverage cooperation between students and researchers to create new scientific relationships. The proposed collaboration focuses on chronic kidney disease (CKD) and the biomarkers that link to cardiovascular events (CVE), which is the main complication occurring in these subjects. We currently have over 700 CKD patients' clinical records concerning disease status and CVE incident documentation. This is a great opportunity for a student with skills in clinical data analysis who is willing to work with us to further identify additional causes that can be influencing CVE in these patients.

Link with the Sustainable Development Goal(s) and the global EU GREEN vision

This project falls under Sustainability Development Goals (SGD) 3, 12, and 17. Primarily, good health and wellbeing target 3.4.1, addressing premature mortality from non-communicable diseases. The purpose of our project is to identify biomarkers that aid in the prevention of early mortality and premature ageing of CKD individuals, mostly due to potentially preventable CVE. This project also falls under SDG 12.7, to ensure sustainable consumption and production patterns. The SDG 12.7 aims to promote public procurement practices that are sustainable, in accordance with national policies and priorities. Identifying potential drug targets and disease pathways has the potential to develop a more personalised medicine approach to treat CKD patients, which will result in less healthcare resource waste and increased sustainable practices in medicine procurement. Additionally, this research internship will coincide with Partnership for the goals, SDG target 17.16.1, by enhancing the global partnership for sustainable development through multi-stakeholders by sharing knowledge and expertise through the international partnerships of EU Green universities.

Topic of the internship and mission of the student

Traditional markers of CKD only stand out when kidney damage is advanced, but early identification of CKD is important to improve patients' survival and reduce associated comorbidities, particularly of CV nature, hence the need for novel biomarkers. Our recent research (see [summary-gervasinig-set.txt](#)) has identified new genetic and non-genetic markers in different pathways related to CKD that are able to impact the speed of disease progression as well as the incidence of CVE. A promising candidate in this regard is the genetic variability found in adrenoreceptors, which we will study in patients with diabetic nephropathy (DN), one of the most common causes of CKD.

Sympathetic nervous system (SNS) overactivity is a well-recognized feature of CKD, including DN, and it plays a central role in the high CV burden of this population. Excess catecholamine signaling contributes to sustained hypertension, left ventricular hypertrophy, arrhythmia susceptibility, endothelial dysfunction, and accelerated kidney decline – all major drivers of CV events. β -adrenergic receptors (encoded by *ADRB1*, *ADRB2* and *ADRB3* genes) are the key transducers of SNS activity in the heart, vasculature, adipose tissue, and kidney, and common genetic variants in these receptors can modify their signaling efficiency and down-regulation. Thus, in patients with DN – a state of heightened SNS activation – genetic variability in adrenoceptors represents a biologically plausible factor influencing CV outcomes.

We have already performed next-generation sequencing in 550 DN patients for the *ADRB1-3* genes, so genetic data for all participants are already available. In addition, general biochemistry of patients at various stages of the disease, clinical records, and CVE incidence will also be available. CKD stages were assessed using the KDIGO classification method and CKD-EPI formula. Renal function was assessed through Proteinuria and albuminuria values. Clinical records contained data regarding patient's hypertension, CVE history, diabetes, and smoking status. CVE were defined as patients records of CVE during follow-ups, documenting CVE as death from CV cause, acute myocardial infarction, acute coronary syndrome, coronary catheterization requiring angioplasty, coronary bypass, typical angina with positive stress tests, sudden death, stroke, peripheral artery disease and lower limb ischemia.

The student will:

- Work with crude genetic sequences to extract information of the genetic variants present.
- Perform multivariate analyses to establish associations between the identified variants and the incidence of CVE in the study population.

Training provided: Performing eQTL analysis to assess functionality of novel variants, establishing the variants effect on DNA binding sites through DNA-seq analysis, learning how to utilize bioinformatics techniques to assess functional consequences of novel variants.

Conditions of Internship:

The selected student will have the opportunity to live in Badajoz, Spain for the duration of their internship, and collaborate with their peers at the University of Extremadura. Learn essential genomic and analytical skills needed to advance their research career and strengthen university relationships for future international research opportunities.