Wit
Welcoming
International
Talent

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under Marie-Sklodowska Curie grant agreement No 101034285

**UNIVERSITY: CIMA University of Navarre (UNAV)**

**WIT PROGRAMME´S RESEARCH LINE NAME:** Unraveling the molecular signature of heart failure with preserved ejection fraction (HFpEF). Insights from liquid biopsy analysis

**DOCTORAL PROGRAMME:** Doctoral Program of applied medicine and biomedicine https://en.unav.edu/web/doctoral-program-of-applied-medicine-and-biomedicine

**COMPLETE DESCRIPTION OF THE LINE**

HFpEF, with an increasing prevalence and dire prognosis, is an unmet medical need as it remains poorly understood and lacks specific diagnostic and therapeutic strategies. Microvascular dysfunction, inflammation and fibrosis emerge as key players in the progression of this pathology. Our objectives are: 1) Exploiting the potential of serum liquid biopsy in HFpEF patients through high-throughput "omic" screenings including next generation sequencing of mRNA (mRNA-Seq) and microRNAs (microRNA-Seq) from endothelial extracellular vesicles and targeted proteomics (proximity extension assay technology); 2) Understanding the role of the identified targets through experimental in vitro and in vivo models and cardiac biopsies from HFpEF patients; 3) Validating their potential as clinical biomarkers in combination with state-of-the-art cardiac magnetic resonance analyses in HFpEF cohorts. This study is part of the European Commission-funded CRUCIAL international project.

Wit
Welcoming
International
Talent

This project has received funding
from the *European Union's Horizon 2020*
*research and innovation programme*
under Marie-Sklodowska Curie
grant agreement No 101034285

**RESEARCH GROUP NAME: Myocardial Remodelling and Heart Failure**

**COORDINATOR:**

- Last and first name; link to the "Portal of scientific production": González Miqueo, Arantxa
  https://cima.cun.es/investigacion/personal-investigacion/arantxa-gonzalez-miqueo

  Department: Program of Cardiovascular Diseases
- Email: amiqueo@unav.es
- Telephone number: +34 948 194700 (Ext. 813023)

**MEMBERS OF THE LINE RESEARCH:**

Dr. Javier Díez Martínez

Dr. Begoña López Salazar

Dr. Susana Ravassa Albéniz

Dr. Gorka San José

Dr. Carmen Roncal Mancho

**ANOTHER RESEARCH LINES OF THE GROUP:**

Role of myocardial fibrosis and increased stiffness of the extracellular matrix on cardiac function in patients with HFpEF and with the associated comorbidities (e.g. diabetes, hypertension, chronic kidney disease, aortic stenosis, atrial fibrillation…) . This line is focused on evaluating the molecular mediators

This project has received funding
from the *European Union's Horizon 2020*
*research and innovation programme*
under Marie-Sklodowska Curie
grant agreement No 101034285

involved in myocardial fibrosis in HF to identify new pathophysiological targets and develop potential therapeutic agents.

Characterization of myocardial remodelling in HFpEF associated with diabetes. Study of the cardioprotective role of the inhibitors of the sodium-glucose cotransporter-2 (iSGLT-2). Diabetes mellitus is one of the risk factors associated with HFpEF. A new type of treatment developed for diabetes, the iSGLT-2, has shown promising cardioprotective effects. This project analyses in depth myocardial remodelling in diabetic HFpEF patients and includes the CARDIASTIFF clinical trial evaluating the cardioprotective effect of dapagliflozin.

Study of microvascular dysfunction as a common causative mechanism in HFpEF and cognitive impairment. This project combines experimental studies in models of HFpEF and cognitive impairment with the clinical development of blood biomarkers and imaging biomarkers (derived from cardiac magnetic resonance) to evaluate the degree of microvascular dysfunction in these patients.

Biomarkers for the implementation of precision medicine strategies for the management of cardiovascular disease. This line is focused on developing a panel of non-invasive biomarkers (biochemical and imaging) to achieve a more accurate and personalized phenotyping, risk stratification and therapeutic management of patients. We have several ongoing projects in this context.

Personalized assessment of cardioembolic risk (PACER-1 clinical trial). Atrial fibrillation and atrial remodelling are important risk factors of stroke. This study aims at developing a panel of biomarkers to identify patients at high risk of suffering a cardioembolic stroke. In order to do so we combine cutting-edge imaging techniques (echocardiography and cardiac magnetic resonance) with liquid biopsy analysis (net generation sequencing of mRNA and microRNAs in extracellular vesicles, proteomic analyses and biochemical biomarkers).

Unraveling the molecular signature of cardiorenal syndrome. Chronic kidney disease is a highly prevalent disease closely associated with heart failure. In this project we perform a liquid biopsy analysis in order to establish molecular

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under Marie-Sklodowska Curie grant agreement No 101034285

patterns for a better stratification of patients, as well as to identify novel pathophysiological mediators in this syndrome.

Evaluation of short and medium term cardiovascular damage following SARS-CoV2 infection with a panel of circulating biomarkers.

- Entities involved in research lines and contact person:

✓ Academic entities:

- Hospital Universitario German Trials y Pujol (Barcelona, Spain), Departamento de Cardiología. Prof. Antoni Bayés-Genís
- Hospital General Universitario Gregorio Marañón (Madrid, Spain), Departamento de Cardiología, Prof. Javier Bermejo
- St. Bartholomew's Hospital, University College London, (London, U.K.)Dr. Thomas Treibel
- Université de Rouen, Institut national de la santé et de la recherche médicale (INSERM). (Rouen, France) Dr. Ebba Brakenhieln
- Katholieke Universiteit Leuven (Lovaina, Bélgica) y Maastricht University (Maastricht, The Netherlands) Dr. Elizabeth Jones
- Institute of Molecular and Translational Therapeutic Strategies at Hannover Medical School (Hannover, Germany). Prof. Thomas Thum
- Centre Hospitaliere Universitaire Nancy, INSERM (Nancy, France). Prof. Faiez Zannad

- Group review

We are a multidisciplinary biomedical research group with a long-standing background in the study of myocardial remodeling, which plays a key role in the development and progression of chronic heart failure (HF). Our research is

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under Marie-Sklodowska Curie grant agreement No 101034285

focused on unraveling the molecular mechanisms involved in HF to identify novel therapeutic targets, and on validating non-invasive biomarkers with diagnostic and/or prognostic clinical value. With this approach we intend to promote the implementation of precision medicine strategies in HF management. In the last 5 years we have participated in over 80 scientific publications, including the most relevant journal of the cardiovascular field. The group has an extended network of National and International collaborators and is involved in European Commission-funded projects. The group also belongs to the Spanish Network of Cardiovascular Biomedical Research (CIBERCV) and to the Health Research Institute of Navarra (IdisNA).

- Link of the group to the "Portal of scientific production"

  https://cima.cun.es/en/research/research-programs/research-programs-cardiovascular-diseases/research-group-heart-failure